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USE OF DRUGS AT 'RAVES'

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Abstract: *Widespread use of drugs at the currently popular 'raves' has caused concern principally because of an increasing number of cases of serious toxicity and even death. The availability and use of drugs at raves, mainly in the Edinburgh area, have been investigated and self-reported use of drugs compared with results of urine screening. Use of Ecstasy and LSD have been confirmed and there is evidence to support the use of Khat. A new preparation, Herbal Ecstasy, is readily available at Edinburgh raves and appears to be widely used. All urines tested positive for one or more drugs or drug metabolites and in general analytical results correlated well with self-reported use of drugs.*

Key Words: Raves, recreational drugs, urine drug screening.

A 'rave' is a dance event where music is played non-stop for several hours and the dancing is hard and fast. Raves are held in a hypnotic atmosphere produced by bright flashing lights and distinctive music which is extremely loud and repetitive and features strong complex percussion patterns. The music can take several forms including *Techno, House, Garage, Hard-core,* and *Jungle,* distinguished by the speed and rhythm. Rave dances are currently very popular with persons in the 16-25 age group.

There has recently been considerable concern expressed in the popular press and in medical journals about the number of cases of serious toxicity and even death as a result of use of drugs, particularly Ecstasy, at raves.[1-4] Ecstasy (MDMA, 3,4-methylenedioxymethamphetamine) is still widely used, but other drugs including Khat, Herbal Ecstasy and LSD (lysergic acid diethylamide) are becoming increasingly popular.

There is also evidence of the use of Eve (MDEA, 3,4-methylenedioxyethamphetamine) .

LSD (Lysergic acid diethylamide)

LSD or 'acid' was a popular drug in the hippy culture of the late 1960's in the UK.[5] Widespread use of LSD then decreased from this time until the late 1980's when it was used in 'acid house' parties and 'rave' cultures. After this period, use of LSD again declined but statistics indicate a resurgence of its misuse in certain areas of the UK.[5]

LSD is usually taken in order to have a unique experience which involves heightened awareness, pleasure, disorientation and hallucination; this is known as 'tripping'. While the effects are sometimes pleasant, a bad 'trip' can be upsetting. Users may also experience hallucinatory 'flashbacks' — spontaneous recurrences of the trip may occur for months after LSD use.[6]

Physiological changes include increased blood pressure, and heart and breathing rate.[6] The most prominent effect is the change in sensory perception including distortion of size and distance, and loss of time sense; visual images and hallucinations appear to move kaleidoscopically.[6] Use of LSD contributes to fatalities and trauma, such as when the user jumps out of a window in order to 'fly'.

LSD is sold as 'blotters' printed with designs such as planets, penguins and strawberries. One 'tab' costs about £3-5. Sale of the material is illegal and usually it is difficult to purchase at raves.

Most of the ingested LSD is extensively metabolised and only a small amount of unchanged drug appears in the urine. RIA is the only immunoassay currently available for detecting LSD although it can be detected by chromatographic methods mainly based on GC-MS.

Ecstasy (MDMA)

In the 1990's, Ecstasy became readily available in the U.K. where it was used as a recreational drug particularly at raves. Apart from a mild amphetamine-like stimulant effect, Ecstasy induces a feeling of euphoria and benevolence, and although it tends to enhance perception, its hallucinogenic potential is low.[1]

At raves the pharmacological effects of the drug may be compounded by physical exertion, and malignant hyperthermia which may be exacerbated by severe dehydration due to lack of access to fluids[1]. Several deaths and severe reactions including hyponatraemia, convulsions, rhabdomyolysis and acute renal failure after use of Ecstasy as a dance drug have been reported.[2]

There is a rare association between hyponatraemia and Ecstasy ingestion.[3-7] The cause is unknown but the rapidity of onset and reversal suggests a potential mechanism is the release of stored arginine vasopressin from the posterior pituitary. Following reports of deaths from malignant hyperpyrexia at 'raves', MDMA users have been advised to drink large quantities of water. However, in the presence of SIADH (syndrome of inappropriate antidiuretic hormone secretion) this could lead to rapid hyponatraemia which could result in permanent neurological damage and even death.[7]

Ecstasy is sold as white tablets often imprinted with designs such as a white dove. Tablets costing £10-15 are usually obtainable at raves.

Urines containing MDMA should give a positive test with EMIT d.a.u. amphetamines assays although the polyclonal assay is reported to be relatively insensitive for the detection of MDMA and MDEA.[8] Unambiguous identification of MDMA can be achieved by chromatographic methods.

Herbal Ecstasy

A marketing leaflet describes Herbal Ecstasy as a new product containing a number of herbs from around the world. These herbs are said to include *Tibetian Ma Huang, Chinese Black*

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Ginseng Root, German Wild Ginko Biloba, African Raw Cola Nut, Wild Brazilian Guarana, Indonesian Green Tea Extract, Russian Golu-Kola, Australian Fo-Ti-Tieng and *Rou Gui* (rare form of Chinese nutmeg). The marketing leaflet claims that effects include "increased energy levels, euphoric stimulation, tingly skin sensations, enhanced sensory processing, increased sexual sensations and mood elevation". The "100% natural and herbal product" is claimed to have "no side effects and detoxifies your entire system whilst producing a range of pleasureable effects".

All of the herbs in Herbal Ecstasy are mild stimulants although some also have other uses in herbal medicine. The major known constituents of Ma Huang (*Herba Ephedrae*) are ephedrine, pseudoephedrine and related compounds.

It has a diaphoretic effect, it is used for chills and fevers, and to promote urination and reduce oedema.[9] Three cases of ephedrine toxicity with temperature elevation, epigastric pain, nausea and vomiting have been reported after ingestion of as little as 15ml of a 1% solution of the herb.[9] Ginko Biloba expels phlegm, stops wheezing and coughing, and stops discharge especially from damp heat.[9,10] It is used for treatment of frequent urination, urinary incontinence and spermatorrhoea. When taken in excess it may cause headache, fever, tremors, irritability and dyspnoea.

Fo-Ti-Tieng promotes general well being and is used as a female tonic.[9] Its use is contraindicated during pregnancy and lactation unless prescribed.

Information on the packet describes Wild Brazilian Guarana as "the life force of the Amazon — the powerful but gentle seed that revitalises mind and body". It has been revered for centuries as the legendary sacred food of the Amazon Indians. Rio Amazon Guarana *(Paullinia Cupana)* is rich in Guaranine, a natural and potent nutrient that is assimilated in small amounts over many hours. It is described on the packet as "ideal for those with a demanding day ahead. It supplements our own natural resources and so greatly enhances our joy of life".

Rou Gui is not nutmeg but *Cinnamoni Cassiae (Cinnemonum Cassia)* from the inner bark of Saigon Cinnamon which contains cinnaminaldehyde, cinnamyl acetate and phenylpropyl acetate. It is used for asthma, to promote menstruation and alleviate pain, and is also used for the treatment of boils. Rou Gui is a very safe drug but large overdose can cause respiratory changes and dilatation of auricular blood vessels.[9]

The product in tablet form (blue in colour) is available at Edinburgh raves and costs about £12 for a blister pack containing 10 tablets. Sale of Herbal Ecstasy and Khat is legal in the UK.

Khat

Chewing fresh leaves of the khat plant *(Catha Edulis)* has been a habit endemic to certain regions of East Africa and Southern Arabia for over 4000 years. In Yemen, where khat-chewing is a part of the culture, a standard "chew" involves a heavy meal beforehand to protect the stomach, a quiet, relaxed environment and drinking plenty of water. The khat is not swallowed but spat out.

A marketing leaflet states that khat is said to produce "feelings of euphoria, increased libido, talkativity, excitement, loads of energy and a big khat smile". Ingestion of khat has been practised in the UK for a number of years,[11,12] and is currently available in several forms in the Edinburgh area.

Khat juice is made by blending the plant with water and lemon, and filtering the resulting mixture. It is sold by the glass (about 600ml), and may be flavoured with fruit cordial. Khat tincture is produced by alcohol extraction of the active ingredients from the plant. It is sold in 25ml bottles. The cost of khat juice or tincture is about £3 per glass bottle. Khat is also available in the form of a tea to which lemon or sugar may be added to taste. The tea is reported to be "a refreshing pick-me-up".

The main psychoactive constituent of khat is cathinone which is closely related to amphetamine.[13] Cathinone resembles amphetamine in its action on the CNS and its sympathomimetic effects. Khat can cause mouth ulcers and insomnia; more serious conditions such as heart disease and oral cancer have been reported, but no links have been proven. Cases of khat-induced toxic psychosis have been reported although they occur infrequently.[14] The marketing leaflet warns that khat products should not be taken by pregnant or nursing mothers, people with heart conditions, or anyone under 16 years. Cathinone is not a banned or controlled drug in the UK.

The main urinary metabolite of cathinone is phenylpropanolamine (norephedrine), with small amounts of norpseudoephedrine; only very small amounts of unchanged drug appear in the urine.[15] Urines from users of khat give a positive test for EMIT d.a.u. amphetamines assays,[16] and identification of phenylpropanolamine can be achieved by chromatographic techniques. Phenylpropanolamine may, however, be present in urine after taking over-the-counter decongestant preparations containing the drug itself, or ephedrine of which it is a metabolite.

The N-methyl derivative of cathinone, methcathinone is a potent amphetamine-like designer drug.[17,18] It is a psychostimulant and may produce paranoid psychosis, hyperactivity, agitation and depression.

According to addicts, methcathinone is more potent and addictive than other psychostimulants and it has intoxicating effects that can last for up to six days. Methcathinone has been reported to be responsible for numerous drug overdose deaths within the former Soviet Union.[17] The drug is abused in the USA. and is in Schedule I of the Controlled Substances Act.

Illicit methcathinone is thought to be racemic and to be metabolised mainly to ephedrine and pseudoephedrine. In addition some demethylation and reduction to phenylpropanolamine and norpseudoephedrine is thought to occur. Urines from methcathinone users should give positive tests for EMIT d.a.u. polyclonal amphetamines assay but ephedrine and pseudoephedrine have low cross-reactivities with the EMIT d.a.u. monoclonal assay.[16]

Eve (MDEA)

In the UK, MDEA is used almost exclusively as a "dance drug". It may be present in so-called Ecstasy tablets or capsules as a substitute for, or in addition to, MDMA.[19]

MDEA has hallucinogenic effects similar to MDMA but there is a dearth of information in the literature about possible harmful effects of the drug. A case of MDEA overdose in which the patient had tachycardia, was hypotensive, and markedly hypertonic has been reported.[19]

We investigated the use of drugs at raves mainly in the Edinburgh area, and compared self-reporting of drug use with substances detected in urine samples .

Materials and methods

Specimens

Urines (25) assayed in this study were obtained from drug users (16-25 years) attending raves in the Edinburgh area. Specimens were collected 6-12 hours after ingestion of drugs. In addition, five urines from drug users attending raves in Ayr were analysed. To minimise the risk of infection of staff handling samples, all urines were heated to a temperature of 96°C for 30 minutes in a water bath prior to analysis.[20]

EMIT assays

All urines were screened for amphetamines using the EMIT (Syva Company) d.a.u polyclonal assay adapted for use on the Cobas Bio (Roche Diagnostics) centrifugal analyser.[20] The manufacturer's recommended threshold limit of 300μg/L was used to classify results as positive or negative. Quantitative results were obtained by using multi-point calibration.[20] In addition, urines were screened for benzodiazepines, cannabinoids, cocaine metabolite (benzoylecgonine), methadone and opiates using modified EMIT assays and thresholds limits of 200μg/L for benzodiazepines, 100μg/L for cannabinoids, and 300μg/L for the other assays.[20-23]

GC-MS

Confirmation and identification of individual amphetamines was carried out by gas chromatography-mass spectrometry using procedures reported previously.[16]

Results

Twenty one of the young people attending raves reported taking Ecstasy and this was confirmed by the detection of MDMA in urine samples (Table I). In eight of the urines assayed, MDEA was also detected while MDA (a metabolite of MDMA) was detected in six of the urines. Screening of urines from four drug users claiming to have taken Ecstasy failed to reveal the presence of MDMA although ephedrine/pseudoephedrine, phenylpropanolamine and unidentified material were detected. In one sample amphetamine was the only substance detected.

Four of the drug users reported taking Ecstasy, Khat and Herbal Ecstasy and their urine samples were found to contain MDEA, ephedrine/pseudoephedrine and phenylpropanolamine; MDMA was not detected in these samples.

One drug user claimed to have taken only Khat and Herbal Ecstasy but MDEA, ephedrine/pseudoephedrine and methamphetamine, in addition to phenylpropanolamine were detected in the urine sample.

Eight of the rave attenders admitted to taking LSD and Khat, and RIA screening tests for LSD were positive for all the urines provided. In two cases, however, the positive results were not confirmed by HPLC and this was attributed to a low concentration of LSD in the samples. Phenylpropanolamine was detected in seven of these samples.

Of the 30 urines screened for drugs of abuse, 15 were positive for cannabinoids. Benzodiazepines, cocaine metabolite, methadone and opiates were not detected in any of the urines.

GC-MS analysis confirmed the presence of ephedrine and caffeine in Herbal Ecstasy tablets.

Table I
Summary of self-reported drug use and substances detected in 30 urines from rave attenders

Self-reported drug use	No of users	Substances detected in urine
Ecstasy	17	
	1	MDMA, MDEA, MDA
	4	MDMA, MDEA, MDA(trace)
	3	MDMA, MDEA
	2	MDMA, MDA
	1	MDMA, MDA(trace)
	1	MDMA
	1	Amphetamine
	4	P/EPH, PPA, U/M
Ecstasy, Khat and herbal ecstasy	4	
	3	MDEA, P/EPH, PPA
	1	MDEA, P/EPH(trace), PPA
Khat and herbal ecstasy	1	MDEA(trace), P/EPH, PPA, methamphetamine
LSD and Khat	8	
	4	LSD, PPA
	1	LSD (*), PPA
	1	LSD (*), PPA(trace)
	1	LSD, PPA(trace), U/M
	1	LSD

MDMA = 3,4-methylenedioxymethamphetamine
MDEA = 3,4-methylenedioxyethamphetamine
MDA = 3,4-methylenedioxyamphetamine
P/EPH = Pseudoephedrine/ephedrine
PPA = Phenylpropanolamine
LSD = Lysergic acid diethylamide
U/M = Unidentified material
(*) = Positive result for LSD screening test: result not confirmed by HPLC — ? low concentration of LSD

DISCUSSION

Our study revealed that Ecstasy is still a popular drug at raves in this area. Use of the drug was confirmed by urine analysis in 12 of the 30 cases studied. In three of these cases the presence of MDEA in urine samples indicated the use of Eve in addition to Ecstasy. Another four users claimed to have taken Ecstasy but urine analysis suggested that Eve had been taken instead of Ecstasy. There was no indication of widespread use of amphetamine or methamphetamine at raves.

Of the 13 rave-goers claiming to have taken khat either alone or with other drugs, use of this material was supported by the finding of phenylpropanolamine in 12 of the urines; in five of these urines, ephedrine/pseudoephedrine was also detected.

Phenylpropanolamine and ephedrine/ pseudoephedrine were detected in urines from four subjects claiming to have taken only Ecstasy. This finding could be explained by unreported use of Khat and Herbal Ecstacy and/or methcathinone. Ephedrine/pseudoephedrine was detected in all urines from subjects claiming to have taken Herbal Ecstacy.

This study confirms the use of LSD at raves in the Edinburgh area where eight users reported taking the drug in addition to khat.

In general, analytical results correlated well with self-reported use of drugs although in some cases users were probably uncertain about the nature of materials purchased. Users were unaware of the possible availability of Eve and methcathinone.

This study supports suggested widespread use of drugs by young people attending raves; urines from all 30 subjects were found to contain one or more drugs and/or drug metabolites. It is perhaps surprising, however, that only 50% of the subjects were found to be using cannabis. Negative results for urine tests indicated that benzodiazepines, cocaine, methadone and opiates were not widely used at raves.

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FEASIBILITY OF REDUCING L-THYROXINE DOSE IN PATIENTS WITH A SUPPRESSED SERUM TSH

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Abstract: *A total of 748 patients on L-thyroxine with a suppressed serum TSH were requested to reduce their dose and this was achieved in 601 patients. Thyroxine dosage was reduced by 25 or 50μg of L-thyroxine and patients were reviewed six months later. Of all 601 patients, 54.4% remained with a suppressed serum TSH despite dose reduction and in 5.8% an elevated serum TSH resulted. 25μg reductions and 50μg reductions were equally likely to result in an detectable but non-elevated serum TSH (42.8% vs 34.1% ns) but 25μg reductions were less likely to result in an elevated serum TSH (3.8% vs 10.0% p<0.01). Only 7/601 patients in the study (1.2%) appeared to require a dose of over 150μg. If dose reduction is thought to be necessary for patients with a suppressed serum TSH, we would recommend 50μg reductions if the original dose is 200μg or more, and 25μg reductions if the original dose is 175μg or less.*

Key words: L-thyroxine, dose, TSH, osteoporosis.

Introduction

For patients on L-thyroxine replacement the risks of under treatment are well recognised, and can be avoided by ensuring that the serum TSH does not remain elevated. The risks of possible over treatment however are debatable. Initial studies suggested that patients on L-thyroxine long-term, and especially those with a suppressed serum TSH (<0.05mU.l^{-1}), were at risk of continuing bone loss,[1,2,3] but more recent work has not confirmed this.[4,5,6] However, mainly because of concerns about possible osteoporosis, many physicians, including the American Thyroid Association have advised that serum thyroxine and serum TSH concentrations should be "normalised".[7,8]

Audit of our thyroid register revealed that 58.5% of our patients on L-thyroxine had a suppressed serum TSH.[9] If a suppressed TSH is a risk for osteoporosis then many of our patients are at potential risk and instituting a dose reduction and necessary subsequent monitoring will have major resource implications.

The aim of the present paper was to assess the feasibility of achieving a detectable but non elevated serum TSH by dose reduction in a patient on L-thyroxine with a suppressed serum TSH. This has been assessed using data from the Tayside Thyroid Register.

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