

Trapped in the 'K-hole'; overview of deaths associated with ketamine misuse in the UK (1993-2006)

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Abstract

Medical use of ketamine has a good safety record, but recent increase of misuse is worrying. We focussed on ketamine misuse mortality figures (UK; 1993-2006), extracted both from St George's np-SAD database and from published mortality statistics. The 23 victims (typically males, in the 25-44 age group) self-administered themselves with a miscellany of psychoactive compounds and alcohol. Ketamine was detected in 4 cases on its own. Although drug identification does not necessarily imply direct contribution to death, the suggested ketamine high safety profile is here questioned. Coroners/ procurators fiscal should consider more routine screening for ketamine in unexpected deaths.

Key words: ketamine; drug related deaths; drug misuse; drug mortality; np-SAD

Declaration of interest: nil

Introduction

Ketamine is a non-competitive glutamate N-Methyl-D-Aspartate receptor (NMDA) antagonist. Although used as a general anaesthetic primarily in veterinary practice (Smith et al, 2002; Wolff and Winstock, 2006), it is occasionally administered to humans as well (BNF, 2006).

Recreational use of ketamine started during the early 1970s in California and, during the 1990s, ketamine was initially sold in the UK as 'ecstasy' (Schifano et al, 2006). HM Customs and Excise reported an emerging trend of ketamine importation into the UK during the last few years (ACMD, 2004). A self-selected readers' survey of a magazine aimed at clubbers found that during the period 1999-2003 ketamine lifetime prevalence increased from 25.5% to 39.8%, whilst current use increased from 3.9% to 16.0% (McCambridge et al, 2007). When misused, ketamine can be injected, sniffed or smoked. Analysis of both London and Manchester clubs' amnesty bins contents showed that ketamine might be the third drug of choice after cocaine and amphetamine (Kenyon et al, 2005). Increased risk for previous-year use of ketamine (OR = 8.26) was recently found among 2.5% of 590 Canadian students who self-identified as gay, lesbian, or bisexual (Lampinen et al, 2006). At present, in the UK, possession of ketamine for personal use is not an offence; its legal status is class C (ACMD, 2004).

At low doses, ketamine stimulant effects predominate. With higher doses, its psychotropic effects range from referential thinking, dissociation and depersonalization to psychotic experiences and include a sensation of feeling light, body distortion, absence of time sense, novel experiences of cosmic oneness and out-of-body experiences, often called the 'K-hole' (Pomarol-Clotet et al, 2006). In long-term exposure, tolerance, dependence, withdrawal signs and flashbacks are described. Schizotypal symptoms and perceptual distortions may persist after cessation of ketamine use (Morgan et al, 2004).

Due to its sympathomimetic activity, ketamine causes mild stimulation of the cardiovascular system, pupil dilation and bronchodilation and does not suppress respiration and gag reflex. Due to these characteristics, ketamine use in medical and veterinary settings has a good safety record (Wolff and Winstock, 2006). Conversely, administration of the drug in high doses can cause cardiovascular and respiratory toxicity (Smith, 2002) and the increase in its unregulated use outside controlled environments may be a cause for concern. In fact, recreational ketamine users may experience numbness of the limbs, analgesia, change in the body temperature and vomiting. There is a risk that the user can choke

on his vomit. Difficulty with balance, combined with numbness, muscle weakness and impaired perception can result in falls, trauma or burns (Jansen, 2000). Risks from the setting have also included drowning, death by hypothermia from lying outside in winter, traffic accidents and becoming a crime victim (e.g. 'date rape'; Jansen, 2000; Smith, 2002; Scott-Ham and Burton, 2005). Despite the reported increased use of ketamine as a recreational drug, relatively few reports of fatalities attributed to ketamine poisoning, either alone or in combination, have been documented. Gill and Stajic (2000) reviewed 87 ketamine-positive deaths occurring in New York City over a two-year period (1997 to 1999), but only 12 were non-hospital deaths due to acute polydrug misuse intoxications. In no instance was a fatal intoxication caused exclusively by ketamine. Between 1978 and 1997 the Institute of Legal Medicine in Hanover, Germany, examined 17 fatal autoerotic deaths, all involving males with an average age of about 37 years. Apart from ketamine, other compounds identified at post mortem included: alcohol, chloroform and a propane-butane gas mixture (Breitmeier et al, 2003).

Because of the paucity of ketamine misuse mortality data, the aim of this report was to focus on those figures that were available for the UK (1993-2006).

Methods

To gather together all the available ketamine misuse mortality figures, two different approaches were combined: a) data were extracted from the National Programme on Substance Abuse Deaths (np-SAD) database, St George's, University of London for the time frame July 1997-December 2006; b) data based on drug-poisoning mortality statistics published by the General Register Offices (GROs) for England/Wales and Scotland were collected, together with data provided to the np-SAD by the GRO for N Ireland from January 1993 to December 2006. Since its inception, the np-SAD has been regularly receiving coroners' information on drug-related deaths amongst both addicts and non-addicts in the UK. To be recorded in the np-SAD database, cases must meet one or more of the following criteria: presence of one or more psychoactive substances directly implicated in death; history of dependence or abuse of psychoactive drugs; presence of controlled drugs at necroscopic examination. The coroners' response rate has been estimated to have been as high as about 90-95% (Ghodse et al, 2006).

Ketamine-related deaths were defined here as: "text search identified ketamine written in the coroner's report (other illegal drugs may also be written)". Data from np-SAD were not included in the total number of cases derived from other records. Cases where ketamine was present as a result of being administered for medical reasons were excluded from this study.

Results

We identified 23 deaths in the UK during the period 1993-2006 where ketamine was mentioned, either on the death certificate or in the np-SAD coroners' report. Eighteen cases were notified directly to the np-SAD (Table 1) and a further 5 cases were identified from GRO sources. Aggregating the information for these two sources of data, we found that these deaths mostly occurred in the 1999-2006 time-frame, with numbers increasing over time. Most victims were males (19/23) and in the 25-44 age group; 21 cases were recorded in England and Wales. At post mortem toxicological examination, ketamine was detected in 4 cases on its own. For these cases, poisoning was the cause of death in all cases and the coroner's verdict was accidental in 3 cases and suicide in 1 case. In the remaining victims, alcohol (8 cases), opiates/opioids (10 cases), benzodiazepines (7 cases), and cocaine (6 cases) were mostly identified here in conjunction with ketamine. Most (13/18) of the subjects notified to the np-SAD were known as drug addicts.

Discussion

To the best of our knowledge, the present report constitutes the largest available collection of ketamine misuse mortality data from both the UK and elsewhere. In this report, we described 4 cases where ketamine was detected on its own, somewhat questioning the ketamine high safety profile suggested elsewhere (Degenhardt, 2005). Most of the cases involved a miscellany of different compounds and alcohol suggesting that, in combination with other drugs, ketamine lethality risk is probably increased. One might wonder if the real cause of death, in polydrug cases, was due to a particular pharmacokinetic interaction and/or to a synergistic effect of the two drugs.

A possible limitation of the present study is given by our definition of ketamine 'related' deaths, which was as comprehensive as possible. The fact that a drug was recorded as being present post mortem does not necessarily imply that it contributed directly to the death. Furthermore, changes in coroners' reporting over time cannot be excluded here.

Ketamine is probably not routinely screened for in toxicology tests (ACMD, 2004). It is here suggested that coroners and procurators fiscal should be encouraged to consider more routine screening for ketamine in unexpected deaths.

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Table 1: Summary results for 23 ketamine cases notified to either the National Programme on Substance Abuse Deaths (np-SAD; 18 fatalities) or the General Register Offices (GROs) occurring in the UK (1993-2006)

np-SAD Variable	np-SAD Results
Year of death	1999: 2; 2000: 2; 2001: 1; 2002: 3; 2003: 1; 2004: 2; 2005: 4; 2006: 3
Gender	Male 16; Female 2
Age (years)	Average = 32.74; range: 19.8- 49.4. 15-24 = 4; 25-34 = 9; 35-44 = 3; 45-54 = 2
Ethnicity	White = 17, Not known = 1
Country of birth	England = 13; Scotland = 2; Germany = 1; Spain = 1; USA = 1
Occupation	Employed (manual = 3; non-manual = 9); unemployed = 5; student = 1
Living arrangements	With others = 10; alone = 6; squat = 2
Addiction/drug abuse history	Yes = 13; No = 2; Not known = 3
Prescribed medication	Yes = 6 (including methadone in 1 case and diazepam in 2 cases); No=6; Not known=6
Region of death	Greater London = 9; Merseyside = 2; Derbyshire = 1; Dorset = 1; Hertfordshire = 1; Nottinghamshire = 1; Surrey = 1; Brighton & Hove = 2
Incident site	Home = 8; other specified residential place = 2; industrial site = 1; place of recreation = 1; river = 1; Not known = 5
Cause(s)/Mechanisms of death	<ul style="list-style-type: none"> • Ketamine & methadone toxicity • Bronchopneumonia, hypoxic brain damage, cardio-respiratory arrest due to drug toxicity • Combined GHB, amphetamine & ketamine toxicity • Drug abuse, bronchial asthma • Drug overdose (morphine & ketamine) • Ketamine & alcohol poisoning • Opiate poisoning • MDMA & ketamine overdose • Drowning • Complications of mixed drug intoxication, due to ingestion of alcohol, cannabis, ketamine, diazepam, MDMA and heroin, followed by prolonged unconsciousness • Stab wound to chest • Pulmonary oedema, cardiac arrhythmias and drug intoxication • Heroin poisoning • Cerebral and pulmonary oedema, mixed drug poisoning • Cerebral and pulmonary oedema, cocaine intoxication • Respiratory depression, multiple drug poisoning • Ketamine toxicity • Ecstasy, ketamine and GHB toxicity
Drugs present at post mortem	<ul style="list-style-type: none"> • Alcohol, methadone, ketamine; • Ecstasy, morphine/diamorphine, opiates, ketamine, benzodiazepines; • Amphetamine, ketamine, ecstasy, cannabis, GHB; • Alcohol, amphetamines, ketamine; • Ethanol, ketamine, morphine; • Alcohol, ketamine, cannabis; • Morphine, ketamine, cocaine, codeine; • MDMA, ketamine; • Diazepam, ethanol, ketamine, temazepam, opiate-type substance; • Alcohol, cannabis, ketamine, diazepam, MDMA, heroin; • Ketamine only (x 2); • Ecstasy, ketamine, ephedrine; • Heroin, ketamine, temazepam; • Ethanol, cocaine & metabolites, ketamine, morphine; • Cocaine & metabolites, diazepam & metabolites, ketamine, cannabinoids; • MDMA, MDA, methylamphetamine, ketamine, amphetamine, cocaine & metabolites, cannabis metabolites; • Ecstasy, ketamine, cocaine, GHB.
Circumstances of death	Whilst drinking with others (x 2); whilst clubbing with others; injecting

	with partner; snorted whilst with others; collapsed during illegal rave; drowned; taken prior to killing himself with a knife; took with a range of other stimulants before engaging in gay sex with group of new acquaintances; overheated whilst wearing rubber body suit; took to excess trying to calm herself down; consumed range of drugs over period of 2 days at various gay venues. Not known = 6
Verdict	Accident /misadventure = 11; open = 2; suicide = 1; dependent abuse of drugs = 1; abuse of drugs = 1; non-dependent abuse of drugs = 1; self-administered overdose of drugs = 1
Additional cases from GRO sources (1993-2006)	<p><i>England & Wales - ONS data</i> Three deaths in the period 1993-2002. All died of accidental poisoning. 2 males and 1 female; ages within the range 20-49 years. Drugs mentioned: 2 x ketamine alone; 1 ketamine + co-proxamol</p> <p><i>Scotland (1994 to 2006)</i> A 26 year-old female, died in 1997. Cause of death recorded on the death certificate as: 1a - septic shock syndrome; 1b - buttock abscess; 1c - chronic drug abuse. Toxicology identified: ketamine, lignocaine, diazepam, temazepam, morphine</p> <p><i>Northern Ireland (1997-2005)</i> A 35 year-old male, died in 2001. Cause of death recorded on the death certificate as: 1a - aspiration of vomit; 1b - poisoning by ketamine, temazepam and alcohol.</p>