Early-warning system: new drugs and emerging drug trends in Europe (promises and pitfalls)

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Outline of talk

- EMCDDA and the Early-warning system on new drugs
- Few examples from the EWS: new drugs, ‘old’ drugs, no drugs
- A new trend: GHB and its precursor GBL
- What have we learned?
Early-warning system: sources and response

Indicator-based

KE Indicators

Core data

Event-based

Reitox EWS

Europol

Early-warning

Warning new drugs

Public health warning

(information relevant to users and care providers)

Adapted from R. Kaiser at al., 2005
Early-warning system (EWS): a truly multidisciplinary effort

EWS is a combination of rapid exchange, collection and appraisal (input - analysis/validation - output) of information over a short period of time; longer-term monitoring of new drugs (market/availability, use, consequences); emerging trends

- Monitoring (routine information collection over time)
- Rapid appraisal of potentially harmful substances
- Intervention (early warning)
EWS: warnings

- New substances (primarily): 4-MTA, PMMA, mCPP, BZP, BDF, DOI, DOC

- Uncommon scheduled/controlled drugs: PMA, DOB, DOM, psilocin

- Unusual adulterants of controlled substances: cocaine-atropine

- Problems with established drugs, e.g. dosage units (tablets, etc.) containing unusually large amounts of active substance, combinations, impurities, contamination, etc: MDMA, GHB, Fentanyl, cannabis

- Dosage units, packaging not containing any psychoactive substances but fraudulently presented as drugs: 2,4-D (pesticide)
m-Chlorophenylpiperazine (mCPP): dosage units

Tablets known in different European countries as:

X4’ (Netherlands, Sweden), ‘duhovka’ (Hungary, Czech Republic), ‘regenboogies’, ‘arc-en-ciel’ (Belgium), ‘arlequin’ (France), ‘rainbow’ (Slovenia), Rolls Royce’, ‘smarties’ (Switzerland)
DIMS – Trimbos institute

% XTC-pills containing mCPP

- 2004
- 2005
- 2006

- mCPP
- mCPP + MDMA

www.emcdda.europa.eu
The chemical 2-(2-methyl-4-chlorophenoxy)propionic acids which belongs to the same group as 2,4-D is also known as MCPP, but should not be confused with mCPP (1-(3-chlorophenyl)piperazine).
EWS: contaminated cannabis

• Nov-Dec 2006 reports (EWS and in the media) about of possible health risks from cannabis contaminated with small glass beads (FR, UK, BE, NL).

• Users of this cannabis (variously know as ‘grit weed’, ‘sand weed’, ‘shiny weed’, ‘gritty bud’, etc) were reporting mouth ulcers, sore throats, chest pains and persistent coughs.

• Shiny, glistening herbal material, feels gritty, ‘bubbles’ under cover slip.

• Other samples appeared covered with crystals and sparkled, particularly when illuminated with a strong light.

• Of the cases identified most contained ‘glass like’ beads. But a few contained irregular shaped ‘glass like’ fragments, which may actually be quartz particles
Health risks

• The main risk may be silicosis, which is caused by long term inhalation of very small silica particles typically less than 5 microns in diameter.

• The glass found was mostly larger than this and therefore unlikely to penetrate into the lungs.

• However, there is an unknown danger from inhaling very hot particles, which may also be modified by the high temperature of a burning cigarette.
Why was it put there?

- To help sell poor quality herbal material?
- To remove resin glands which are used to produce ‘skuff’?
- To increase the weight?

Lead contaminated/laced cannabis (Germany, Austria) seems to support the latter explanation. In the beginning of 2008, 29 patients (16-33 years of age) in 4 hospitals in Leipzig area with symptoms of lead poisoning.
EWS: cocaine adulterated with atropine

- Nov/Dec 2004-March 2005 (IT, NL, FR, BE, UK AU); July 2007 (IT)

- Atropine is a naturally occurring alkaloid - anticholinergic agent

- Two EMCDDA alerts Dec 2004 & March 2005, the latter included information on diagnosis and intervention.

- ‘Toxicity: tachycardia, rapid respiration, hyperpyrexia and central nervous system stimulation marked by restlessness, confusion, excitement, paranoid and psychotic reactions, hallucinations and delirium and occasionally seizures. A rash may appear on the face or upper trunk. In severe intoxication, central stimulation may give way to central nervous system depression, coma, circulatory and respiratory failure and death.

- Antidote to atropine is physostigmine or pilocarpine.’
EWS: (3-methyl)fentanyl (Chronicle of a death foretold)

- Large seizure in Austrian (March 2004), Estonia cluster of OD (May 2004); dangerous paper trips, the Netherlands (July 2006).

- ED Tallinn, 2-9 May 04 – app. 100 OD caused by ‘white Persian’, on average 13-15 overdoses case per day (usually ED deals with 30 overdoses case per months).

- 13 deaths related to Fentanyl in Sweden (2003), reported in 2004.

- US epidemic, June 2006 alert CSAT, SAMHSA

- Warning included specific intervention: ‘suspected OD to be treated with Naloxone injection, 0.4-2 mg IV, SC or IM every 2 to 3 minutes which should rapidly reverse symptoms related to a narcotic overdose. If there is no response after 10 minutes, a different diagnosis should be considered. (Naloxone can also precipitate immediate narcotic withdrawal symptoms as overdose symptoms are reversed.)’
EWS: Fentanyl

Source: http://www.blotterart.net/gallery/Blotter-Art-2000-Present/05_G
An epidemic of fatal 3-methylfentanyl poisoning in Estonia

Bilka Oja, Merja Geiergsev, Milana Liv, Aime Riikja, Erkki Vaarli

Abstract An exceptional epidemic of poisonings due to the highly potent opioid designer drug 3-methylfentanyl (TMF) was revealed among Estonian drug users in 2005–2006 by post-mortem forensic toxicology. Quantitative analysis of cis-TMF, trans-TMF, and fentanyl was performed by liquid chromatography-tandem mass spectrometry. Comprehensive toxicological analysis was performed using a multi-technique approach. The number of TMF-related fatal accidental poisonings identified was 46 and 71 for 2005 and 2006, respectively. The proportion of male victims was 91.5% and the mean age of all victims was 26 years at death. TMF was used predominantly by intravenous injection. There was no significant difference in the blood concentrations of cis-TMF and trans-TMF between pure TMF poisonings and mixed TMF poisonings. The mean combined concentration of TMF stereoisomers among pure TMF cases (1.9 μg/L) was more than ten times lower than the mean fentanyl concentration in fentanyl-related fatalities. Concomitant use of other drugs involved alcohol, amphetamines, benzodiazepines, and cannabis, but very rarely other opioids.

Keywords 3-methylfentanyl • Fatal poisoning • Post-mortem • Blood concentration • Designer drug

Introduction

Alpha-methylfentanyl, the first designer drug, appeared on the illicit drug market in California in 1979. In 1984, another fentanyl derivative, 3-methylfentanyl (TMF), was identified and the drug was involved in an epidemic of overdoses in California in 1984–1985 [1]. The first TMF seizures in Russia took place in 1998 in St. Petersburg [2]. The slang terms for alpha-methylfentanyl and TMF include “china white”, “china pink”, “Persian white”, “egg white”, “crocodile”, “dragon”, “999”, and “synthetic heroin”. TMF has so far been involved only in relatively short-lived epidemics [3, 4]. This is obviously due to the high potency of this opioid drug and the associated dosing problems; the cis-(+)-isomer of TMF is approximately 7,000 times as potent as morphine while the trans-(−)-isomer is approximately 1,000 times as potent [5]. Figure 1 shows the chemical structures of fentanyl, alpha-methylfentanyl, and cis- and trans-TMF. The compounds metabolize by Ni-deralkylation with loss of a phenethyl group, TMF yielding nor-TMF whereas alpha-methylfentanyl and fentanyl yielding norfentanyl [6].

According to Europol [7], fentanyl and its derivatives are becoming available in Estonia, Finland, Latvia, Lithuania, Sweden, and countries on the eastern border of the European Union. Fentanyl may earlier have originated mainly from the Russian Federation and Ukraine, but since 2003, experimental fentanyl production has also been reported elsewhere [7]. The Russian Federal Drug Control Service (FSK) has reported a sharp increase in seizures of TMF by Russian law enforcement. In the first 6 months of
Emerging drug trend: E-POD methods

• A picture of an emerging drug trend has to be constructed from a wide variety of ‘leading-edge indicators’ (obtained from sources close to drug users) at regional, city and local levels.

• The EMCDDA is looking at two sources for new leading-edge indicators:
  
  • Hospital emergency units: for information about risks associated with recreational drug use.

  • Internet: for information about consumer trends found in online forums and drug vendor websites.
GHB/GBL: an emerging trend
Drivers of the trend:

- The ease with which GBL can be acquired over the internet allows cheap and easy access.
- Prevalence of GHB/GBL is generally low but is becoming more common in some sub-populations, settings or geographical areas.
- The multi-purpose pharmacological characteristics of GHB and GBL may appeal to a wide customer base, for: relaxation, sexual enhancement, bodybuilding and anti-aging.
- It is often sold as a liquid and is therefore rather similar to alcohol in both its form and effects.

Barriers to the trend:

- Since 2000 drug laws have prevented open sale of GHB.
- Negative effects include vomiting and loss of consciousness, which is particularly problematic in social settings.
- Prevention campaigns have been instigated within the leisure industry to limit the use of GHB and media reports about its use in sexual assault have helped to give a negative image.
Grass Roots and Multiple Sources Approach

Top-Down

Routine monitoring data
Scientific literature (25%)

GHB/GBL

Bottom-Up

Internet, newspaper/media
hospital emergency and ad hoc survey data (75%)
Lessons from the EWS: policy implications

• (Formal) Multidisciplinary networks are important.

• Some new threats have self-limiting dimensions, but others may be here to stay (anticipation).

• Information from law enforcement sources has a particular value.

• Gaps between practice and forensic science should be bridged.

• Early information needs to extend to multiple sources beyond the established prevention, treatment and harm reduction information sources and practices.

• The importance of leading-edge indicators: HE, Internet.
Lessons from the EWS: definition alerts

- Consider risk independently of legal status.

- Consider weighting separately the issues of reliability (quality) of information and relevance (specific risk issues involved such as health).

- Consider a dual definition of risk as probability and degree of seriousness (hazard).

- In relations to new drugs, consider scientific evidence in relation to better-known drugs.
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