

Review Article

Low Self-Reporting of Addictive/Recreative Substances in Overdoses Requires Report of the Results of Toxicological Analysis in Suspected Overdoses

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Submitted: 31 May 2016

Accepted: 29 September 2016

Published: 01 October 2016

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OPEN ACCESS**Keywords**

- Poisonings
- Drugs
- Toxicological analysis

Abstract

Acute poisonings are a common cause of presentation in intensive care units (ICU) while there is no national registry of poisonings in France. Regarding the database we have collected from 2007 to 2012, medicines (81.8%) and addictives / recreatives substances (10.7%) were the most frequently reported substances. The withdrawal of substances exhibiting toxicity in the post-marketing phase occurred frequently, including meprobamate, dextropropoxyphen meanwhile the total number of annually admitted poisoned patients did not decrease. The lack of decrease of the total number of acute poisonings admitted in ICU supports the hypothesis of a mechanism of replacement of toxic drugs by others. In addition the replacement, the database highlighted possible drug-drug interactions that resulted essentially in competition of different substrates to the same cytochrome, far more frequently than inhibition or induction.

Gathering facilities provided by three University Tox Labs resulted in a low added value of TA in medicinal drug poisonings. TA was of limited value for the definitive diagnosis of the majority of medicinal drug poisonings and did not allow clarifying drug-drug interaction. Conversely, TA was highly efficient to unveil the exposure of unreported addictive/recreative substances.

ABBREVIATIONS

IDF: Ile De France; ICU: Intensive Care Unit; TA: Toxicological Analysis; SID: Supposed Ingested Drug

INTRODUCTION

Severe acute poisonings are a frequent cause of admission to the emergency and intensive care services [1], in both developed countries and in developing countries. They result in 14% of the activity of ICUs in Ile de France (IDF) [2].

Today in France, exhaustive data regarding the involvement of various toxicants, including medicinal drugs and addictive/recreative substances in these poisonings is difficult to obtain

with a great likelihood of accuracy. Indeed, during the course of an overdose, the drugs used are frequently self-reported by the patient or his relatives. In contrast, regarding the use of addictive/recreative drugs, there is a tremendous far lower self-report of the spectrum of chemical used in this addictive/recreative behavior. However, knowing the most frequently involved substances is essential to guide the management of poisoned patients and guide the toxicological analysis that could be useful in the diagnosis, prognosis and treatment and even prevention of these serious poisoning [3].

The final diagnosis in acute human poisonings is an ongoing process during the course of the poisoning, starting by collection of information, including on the supposed ingested substance(s)

and the dose(s). In an emergency medical setting, both items are either self-reported by the conscious cooperative patients, or reported by relatives or paramedics in symptomatic patients, ii) Signs and symptoms observed by witnesses, caregivers, paramedics, and attending physicians on arrival to hospital, that usually allows to refine a toxidrome suggestive of a class of chemicals iii) after admission to hospital, effects of antidotes an number of which are specific antagonists, including naloxone and flumazenil as well as iv) the results of toxicological analysis (TA). However, in addition to toxscreen, the definitive diagnosis requires frequently days and even weeks prior emission to final validated results [2].

A mono centric study of intra tertiary university hospital in Paris over a period of six years, from January 2007 to December 2012 on severe acute drug poisonings as defined by a clinical status needed admission to intensive care unit (ICU) during the course of the poisoning. During this period of time, 1971 consecutive stays were collected, medicinal drugs were self-reported in 81.8 % of the cases, addictive / recreational substances were self-reported in 10.7%, and non-drug substances in 2.7% Substances other were unknown in 4.6% [4].

Analysis of the "top 30" of the most frequently reported substances over this period of time showed that ethanol remained at the top in terms of annual frequency of occurrences, followed by paracetamol. There were a predominance of the class of benzodiazepines including alprazolam, bromazepam, diazepam, clonazepam, oxazepam, prazepam, and benzodiazepine-related drugs, including zopiclone and zolpidem.

The annual analysis of the distribution of poisoning over this period allowed the detection of disappearance and appearance effects of a number of substances. However, in 2010 and only for this year, the occurrence of meprobamate was greater than that of paracetamol. As for dextropropoxyphen after official withdrawal in 2010, dextropropoxyphen was still a cause of severe overdose in 2011, suggesting people stockpiled the drug before withdrawal.

The median drug ingested self-reported by the patients was 3. We looked for any possible interaction between drugs used in self-poisoning. The study of interactions was restricted to cytochromes P450 2A, 2D, 2E, 3A and 3C, 27. The most frequent mechanism was substrate competition. In contrast, enzyme inhibition and possible induction were far less frequent. The ratio of magnitude of competition, inhibition, and induction were 10, 1 and 1, respectively [4].

The toxicological analysis remains the gold standard for the definitive diagnosis of poisonings. However, the added value of TA remains unclear in the different conditions of overdoses including medicinal drug and additives/recreatives substances overdose. A retrospective, monocentric, clinical, , and observational study was performed in overdoses admitted between the first of January 2014 up to the 17th of April 2015 using complementary facilities provided by three University Toxicological Laboratory in order to clarify the value of TA.

In this study, the supposed ingested drugs were classified in one of the three following groups:

a. SID+ TA+: In this group we included the occurrences of substances that were self-reported and were found by TA

b. SID- TA+: In this group we included the occurrences of substances that were not self-reported but were found by TA

c. SID+, not searched: in this group we included the occurrences of substances that were supposed ingested by the patient but have not been searched by TA

In the SID+, TA+ group, there were a total of 74 occurrences resulting in 51 occurrences (70%) of medicinal drugs and 23 occurrences (30%) of addictive/recreative substances. In the SID+, not searched group there were 142 occurrences (96%) of medicinal drugs and 8 occurrences (4%) of addictive/recreative substances (Table 1).

The SID-, TA+ group corresponded to the group of substances that were not reported by the patients but were detected by TA. In this group, TA unveiled 263 occurrences resulting in 116 occurrences of medicinal drugs and 147 occurrences of addictive/recreative substances (Table 2).

DISCUSSION AND CONCLUSION

Regarding the medicinal drugs, the three laboratories unveiled substances not supposed ingested by history but ingested at a dose resulting in toxic blood concentrations in 15% of cases of medicinal drugs. These findings suggest a rather low rate of efficiency of analytical toxicology even cumulating the

Table 1: Results of analytical toxicology in terms of detection with and without quantification in response to the supposed ingested addictive/recreative substances.

SID+ involving addictive/recreative substances	TA+	NOT SEARCHED
ACETONE		1
HEROINE		2
CANNABIS	1	
COCAINE	7	1
ETHANOL	13	
GHB	1	2
MDMA	1	1
MEPHEDRONE		1
TOTAL (occurrences)	23	8

Table 2: Addictive/recreative substances that were found by TA meanwhile not being suspected as reported by the paramedics, rescuers, and medically staffed ambulance in comatose patient or not self-reported by the patient in conscious patients.

SID- involving addictive/recreative substances	OCCURRENCES
6 MAM	1
COCAINE	35
ETHANOL	37
MDMA	34
THC	40
TOTAL (occurrences)	147

capabilities of three toxicological laboratories using modern methodology [5].

Conversely, TA using modern technology is highly efficient methods unveiling exposure to unsuspected addictive/recreative substances and provided highly valuable information to the clinician. The added clinical value of hair analysis regarding the recent past history of use and abuse of recreative and addictive substances remained to be assessed.

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Cite this article

Alaywa K, Beller CL, Jouffroy R, Cisternino S, Laprevote O, et al. (2016) Low Self-Reporting of Addictive/Recreative Substances in Overdoses Requires Report of the Results of Toxicological Analysis in Suspected Overdoses. *J Subst Abuse Alcohol* 4(2): 1049.