

Chemical submission: results of 4-year French inquiry

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Abstract Psychoactive substances may be administered without the knowledge of a victim in order to induce incapacitation and thus facilitate criminal actions. The characteristics of the victims and the drugs used in such suspected chemical submissions (CS) were analyzed in 309 cases collected from October 2003 to December 2007 through a national survey. Out of 309 cases, 158 met all criteria of CS. The victims were mostly female ($n=89$, 56%). The type of aggression was mostly sexual assault (in 79 cases 50%). Benzodiazepines and related drugs were detected in 129 victims (82%) and were mostly clonazepam, zolpidem, and bromazepam whereas flunitrazepam and gamma hydroxybutyrate, well known for their use in CS, were identified in 11 (7%) and five (3%) of the 158 victims. CS is not an anecdotal phenomenon in France. Information for health professionals and workers in forensic structures as well as education of the general population associated with preventive measures such as drug dosage form changes should contribute to improved care management of victims and decreased risk.

Keywords Chemical submission · Rape drugs · Drugs criminal use · Benzodiazepines

Introduction

Psychoactive substances (PAS) may favor involuntary actions and their role has been discussed in several trials when the criminal had taken such substances [1]. Conversely, administration of the same drugs without knowledge of the victim in order to induce incapacitation and thus facilitate criminal actions such as robbery or rape has been defined as chemical submissions (CS) [2, 3]. In this situation, the PAS is used as a weapon by the assailant and constitute an aggravating circumstances in their act. Anecdotal cases have been published since the 1980s [4], but the use of chloral hydrate has been known since the beginning of the twentieth century [1].

These substances may induce either a marked depression of consciousness level, and thus a lack of resistance, or a submission with suggestibility, disinhibition, and anterograde amnesia, leading an alert victim to perform acts against the true will. They may be obtained easily by the perpetrator and as they are odorless, colorless, and tasteless and are administered surreptitiously, they are most often incorporated into drinks. They act rapidly and usually for a short period of time. Their chemical detection is often difficult due to their short half-life, their instability, and their low dose [5, 6].

Various drugs and nontherapeutic substances have been involved. Most of them are drugs indicated for psychotropic purpose such as flunitrazepam [7]. Other products have also been reported for use in CS: the anesthetic drugs gamma hydroxybutyrate (GHB) and potentially its precursors, the industrial solvents gamma butyrolactone and 1,4-butanediol [8–11] and ketamine [12], clonidine [13], antihistamines such as doxylamine [14] and anticholinergic alkaloids: either drugs such as scopolamine [1] or Solanaceae plants such as *Datura* and *Mandragora* which contain atropine and hyoscyamine [15].

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Among the victims of a crime such as rape with suspected drug use, a few studies have investigated the prevalence of each drug or illicit product [8, 11, 16, 17]. However, based on some of these studies, it cannot be known whether the substances had been taken voluntarily or with the aim of chemical submission. Among the victims of CS, several studies showed that benzodiazepines were the most frequently identified substances [18–20].

The problem of CS was brought to the attention of the French Health Authority Agency Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) and led it to set up a survey to elicit an inventory of cases and to study the substances involved in this context and the *modus operandi*. This inquiry has already allowed some preventive messages to be addressed to health professionals and to other people especially the young. Preventive measures such as modification of dosage forms of drugs (i.e., addition of colorant or bitter additive) and a summary of product characteristics modifications have been proposed [21].

To allow better care management of victims, AFSSAPS has proposed protocols and some procedures to help all health professionals in this context for care management, sampling, and storage of specimen (Afsaps. Soumission chimique: <http://afssaps.sante.fr/>).

Laboratories involved in this survey must have appropriate equipment and validated competence. Most of them belong to the Société française de toxicologie analytique–French Society of Analytical Toxicology which has worked out a consensus for toxicological investigations of drug-facilitated crimes [22].

We report the result of this study focusing on the characteristics of the victims and the drugs used in suspected CS in cases collected by the French Network of Centers for Evaluation and Information on Pharmacodependence which were mandated by the AFSSAPS.

Methods

This study is based on the voluntary notifications of cases already documented within the medical or forensic structures. Several types of notification sources were involved in the collection of the cases of suspected CS: hospital departments of medicine, forensic emergencies, or departments of forensic medicine and toxicology laboratories.

The subjects included in this study were victims of criminal actions in which at least one substance is suspected to have been administered for CS and were identified through toxicological analysis in various materials (e.g., blood, urine, hair, capsule, drink, or food) or assailant confession. Frequently, for victims, the main reason of complaint or medical consultation was to be drugged without their knowledge. Victims were not included if they were aware of their consumption, i.e., in the case of substance consumption under

threat and voluntary consumption of drugs or nonprescribed substances. The diagnosis of CS is based on the presence of:

1. One aggression (rape, robbery...)
2. At least one PAS which was unknown to the victim (detected by toxicological tests or revealed by assailant confession)
3. Clinical data and chronological parameters consistent with the pharmacology data of that PAS

Based on these criteria, we identified two groups of victims: the first group (A) with full cases in which the diagnosis of CS was incontestable and the second group (B) without all criteria, in which the diagnosis was likely.

The products used for CS were distinguished from substances in which they were added and from drugs taken for a therapeutic use, based on information provided by the patient.

Results

From October 2003 to December 2007, 309 cases were collected in respect of anonymity. Most of them were reported by departments of forensic medicine (140/45%) and by toxicology laboratories (107/35%; Table 1).

The cases are divided into group A including 158 victims and group B with 151 victims.

Group A included full cases with established CS diagnosis. The 158 victims were mostly female ($n=89$, 56%). Mean age was 31.4 years old (2–90 for the 154 with known ages), 23 victims being less than 18 years old. The complaint was lodged in 137 cases (87%). The substance (or vehicle) in which the submission product was added was known by 122 victims (77%) and was an alcoholic beverage in 60 of these cases (49%; Table 2). The clinical symptoms reported were related to the products taken, whether the substance used for CS or the substances in which the product was added, and to the consequences of the assault. The most frequently reported symptoms in 152 victims were amnesia ($n=103$, i.e., in 68% of the victims), consciousness disorders ($n=83$, i.e., in 55% of the victims), and symptoms related to trauma or violence ($n=39$, i.e., in 26% of the victims).

In 131 cases (83%), it was specified whether the victim knew the aggressor or not, and, in 63 of these cases (48%), the aggressor was known to the victim. The sex of the aggressor was specified in 126 cases (80%) and was male in 111 of these cases (88%). The type of the aggression was

Table 1 Sources of notifications (absolute numbers)

Departments of forensic medicine	140
Toxicology laboratories	107
Hospital departments	56
Others	6

Table 2 Substances in which the submission products were added

	Number
Beverage	
Alcohol	60
Nonalcohol	20
Not specified	19
Food	12
Drug	10
Cigarette	3
Not specified	36

In one case, two substances had been ingested
N absolute numbers of substances

a sexual assault in 79 cases (50%) with female victims being more often affected (87%), a theft in 74 cases (47%), a child mistreatment in nine cases (6%), and sedation in four cases (3%) [homicide was the aim in two cases]. In nine cases, both sexual assault and theft were reported.

The time elapsed between the aggression and the medical examination or sampling for toxicological analyses was 12 h or less in 27 cases (17%), 13–24 h in 40 cases (25%), 25–72 h in 52 cases (33%), over 72 h in 29 cases (18%), and not specified in ten cases (6%).

Toxicological analyses were performed with appropriate techniques such as chromatographic techniques which were high-performance liquid chromatography, either coupled to diode array detection (LC–DAD) or to mass spectrometry (LC–MS) or tandem mass spectrometry (LC–MS–MS) or to electrospray mass spectrometry (LC–ES–MS) and gas chromatography coupled to mass spectrometry (GC–MS) or to tandem mass spectrometry [5, 22]. Samples were collected in duplicate by health professionals in the event of second expert evaluation. Blood was collected (3 × 10 mL) in a container with preservatives (EDTA to avoid GHB formation *in vitro*) within 24 to 72 h after the ingestion of PAS accompanied by urine specimen (30 mL). In case of negative results or a long delay, hair sampling was proposed and made approximately 1 month after the fact in laboratories which usually ensure cold storage (for all samples). In case of lodged complaints, samples were sealed and then sent to the laboratories with informed times of taking the specimen.

The distribution of the drugs and of the nontherapeutic substances identified from the chemical analyses or by assailant confession and not related to medication taken under prescription is detailed in Table 3. The main therapeutic class was benzodiazepines (BZDs), detected 149 times in 129 of the victims (82% of all victims). Among BZDs, the most frequently identified drugs were clonazepam ($n=42$), zolpidem ($n=20$), and bromazepam ($n=17$). In seven cases using zolpidem, we describe a serial burglary committed in the same area. The other drugs were antihistamines H1 ($n=16$), neuroleptics ($n=$

11), opioids ($n=8$), anesthetics ($n=6$), antidepressants ($n=3$), and other therapeutic classes of drugs ($n=4$). Nontherapeutic substances used for chemical submission were identified in seven victims and were mainly methylenedioxymethamphetamine (MDMA; $n=4$), cannabis ($n=1$), cocaine ($n=1$), and alcohol ($n=1$).

The substances ingested voluntarily, whether or not the substance in which the product used for chemical submission was added, were alcohol ($n=51$), cannabis ($n=32$), cocaine ($n=7$), and MDMA ($n=3$).

Group B included 151 incomplete cases lacking some criteria. These cases were without:

1. Identified assault (related to amnesias in some cases): $n=68$
2. Accurate context: $n=39$
3. Information on current treatment: $n=61$
4. Chromatographic analysis techniques: $n=21$

All these cases were considered and managed as victims of CS by forensic or medical units.

Despite the lack of information, it was noticeable that the characteristics of the victims were similar to those of group A. Female victims were also most frequent (97 cases/64%) the mean age was 32.8 years old and 7% ($n=10$) were minors. Of the 92 victims, 61% lodged a complaint while 13 refused to do so. Sexual assault was reported in 47 cases and concerned females in about 87%. The victims were managed in less than 24 h in 88 cases (58%). Among the substances which were detected by toxicological analysis, 21 cases had only immunological techniques (immunoassay by Syva Emit II Plus methodology) and concerned BZDs. In two cases, the substance was revealed by the assailant.

The distribution of substances in this group was similar to those of the first group. BZDs were the main substances used in 106 victims (70%). Among the 116 mentioned, clonazepam ($n=18$), bromazepam ($n=16$), and nordiazepam ($n=10$) were the most frequent. Other PASs were detected 57 times, including antihistamines ($n=20$) and GHB ($n=2$). Nontherapeutic substances were used more frequent in group A. Among them, amphetamine and its derivatives were detected in 14 cases, cocaine in three cases, cannabis in two cases; heroin, lysergic acid diethylamide, scopolamine, and ayahuasca were found only once.

Discussion

In accordance with the literature data, the victims were the young females but persons at any age can be affected. In this study, the aggression was not confined to rape but extended to other types of assaults such as robbery or sedation (without therapeutic indication) of children and the elderly with the aim to get peacefulness.

Table 3 Distribution of PAS involved in CS without knowledge of victims

Substances	Number	Delay (h, w, m)	Blood (+)	Urine (+)	Hairs ^a (+)	Vehicle (+)	Other (+)	LC- MS	LC- MS- MS	GC- MS	GC- MS- MS	LC- DAD	LC- ES- MS	CPG- FID
Clonazepam	42	2 to 168 h	39	36	16	2		+						
Zolpidem	20	1 to 110 h	7	11	6	5	1 vomit	+						
Bromazepam	17	12 to 96 h	10	8	5			+				+		
Flunitrazepam	11	1 to 168 h	8	8	4			+						
Zopiclone	9	5 to 120 h	3	3	3	2		+				+		
Oxazepam	9	1.5 to 72 h	7	8	1	1		+				+		
Nordiazepam	9	10 to 72 h	5		4			+				+		
Diazepam	8	2 to 47 h	6	5	2			+						
Alprazolam	4	10 to 108 h	2	3	2			+					+	
Tetrazeepam	4	<24 to 45 h	4	4	2			+						
Lorazepam	3	48 to 67 h	2	2	2	1		+						
Midazolam	3	47 to 72 h	1	3				+						
Loprazolam	2	5 h and 1 month	1		2			+						
Prazepam	2	18 and 45 h	2	2				+						
Triazolam	2	48 h and 4 months	1	1	1			+						
Clobazam	1	48 h	1	1						+				
Lormetazepam	1	12 h	1					+						
Temazepam	1	45 h	1	1						+				
Common metabolite of lorazepam- lormetazepam	1	36 h	1	1						+				
Doxylamine	12	10 to 168 h	6	10	4		1 vomit	+						
Cyamemazine	7	10 to 168 h	5	7	2			+						
Niaprazine	2	<36 h/>1 month	2		2			+						
Alimemazine	2	24 and 40 h	1	2				+						
Hydroxyzine	1	24 h	1											
Cyproheptadine	1	17 h		1							+			
Cetirizine	1	16 h		1										
Mequitazine	1	<12 h	1	1				+						
Propoxyphen	2	8 and 17 h		2						+				
Morphine	2	24 h		2	1	1				+				
Pholcodine	2	>12 h	1	2						+				
Tramadol	1	<12 h		1										
GHB	5	<7 h->2 weeks	1	1	2	1				+				
Ketamine	1	<9		1						+				
Clomipramine	1	50 h	1	1						+				+
Imipramine	1	20 h		1						+				
Citalopram	1	<12 h		1						+				

Phenobarbital	1	62 h	1	1	1	+
Quinidine	3	8 to 20 h	3	3	3	+
MDMA	4	15 to 40 h	3	2	2	+
Cocaine	1	48 h	1	1	1	+
Cannabis	1	19 weeks	1	1	1	+
Alcohol	1	<12 h	1	1	1	+

N absolute numbers of victims, + number of positive samples, *Delay* time elapsed between consumption of PAS and sampling, *LC-DAD* high-performance liquid chromatography coupled to diode array detection, *LC-MS* high-performance liquid chromatography coupled to mass spectrometry, *LC-MS-MS* high-performance liquid chromatography coupled to tandem mass spectrometry, *LC-ES-MS* high-performance liquid chromatography coupled to electrospray mass spectrometry, *GC-MS* gas chromatography coupled to mass spectrometry, *GC-MS-MS* gas chromatography coupled to tandem mass spectrometry, *CPG-FID* gas chromatography coupled to flame ionization detector

^a Hairs were usually collected approximately 1 month after the facts

Concerning the assailants, information on them was very succinct and, even if they were known, the conclusion of prosecution remained unknown because it was not reported to our network.

For PAS, the most frequently identified drugs belonged to the class of BZDs which were detected in 82% of the victims. Clonazepam, bromazepam, and zolpidem accounted for 53% of these substances, whereas flunitrazepam—a benzodiazepine previously well known for its use in CS [7]—was identified in only 7%. This low rate for flunitrazepam may be related to the fact that dosage form properties of this drug were changed in the late 1990s in order to render it detectable in drinks. On the other hand, in France, the prescription and the dispensation of flunitrazepam are controlled as narcotic substance and its use is limited.

In three other studies, the breakdown of the substances involved in suspected chemical submission also showed the predominance of BZDs, identified in up to 80% of the cases [18–20]. The results concerning clonazepam and bromazepam were comparable to those of substances abused in the drug addict community [23]. Additionally, the analysis results of BZDs must be interpreted cautiously, taking into account the data of victim medications. This is important since molecules of some BZDs can metabolize into another substance and mislead the interpretation of certain cases with two or three substances detected on specimen. This is evident in the case of diazepam which is an active metabolite of tetrazepam which of itself is a parent drug of temazepam, nordiazepam, and oxazepam [24].

Other psychotropic substances, less known for their use in chemical submission, also accounted for 24% (e.g., antihistamines, neuroleptic drugs, opioids, antidepressive drugs, and nontherapeutic substances). Conversely, GHB, claimed to be a drug commonly used for rape, was detected in only five (3%) of the victims. This low proportion may have some explanations such as a short initial action and half-life of this anesthetic agent at the origin of negative results of blood and urine in case of late sampling [25]. Currently, the progress of analytical techniques have made possible the quantitative determination of the drug in hair specimen. The study of the GHB concentrations can ascertain its endogenous origin (below 4 mg/l in blood and 10 mg/l in urine) [26]. The second explanation is that, since 1998, GHB is a controlled narcotic substance in France. And therefore its availability outside hospitals is possible only by illicit manufacturing (or via Internet) [3, 6].

Nontherapeutic substances may have been taken in order to enable ingestion of the product of submission but may also have been taken independently. They may have acted synergistically with the substance used for chemical submission. In this study, alcohol and marijuana were identified in 49% and 20% of the victims respectively, a rate similar to that observed in studies of rape victims suspected of drug

use [8, 11, 27]. This alcohol rate reached 77% of victims in other study [16].

Ecstasy (amphetamine and derivatives), though less frequent in our study, has some effects sought by assailants such as disinhibition, modification of emotion and attention, and perception impairment [28].

This study has several limitations.

Firstly, routine immunochemical methods are insufficient to detect all the substances used in cases of CS. In this study, only 21 cases of group B (7% of all victims) had no chromatographic techniques. These incomplete toxicological analysis concerned BZDs and were decided by medical or forensic personnel.

Secondly, although the victims were usually asked about voluntary drug taking, sometimes, this information was lacking in the medical records even if the victim had been managed as a case of chemical submission (this fact could be related to an omission on the notification or really expressed in no current medication). In two American studies of rape victims suspected of drug use from either past history or clinical examination, GHB and BZDs were found in less than 15% and flunitrazepam in less than 3% of the cases. In these studies, the presence of these substances did not necessarily indicate they were used voluntarily by assailants in the rape and may reflect an exposure to the drug before or after the rape [8, 11].

These two points show that thorough anamnesis, early samplings and appropriate analytical tests are optimal in the care of victims. Some information and procedures are required and proposed to recognize CS cases and improve the management of victims [3, 6, 29].

Furthermore, this study focused on the substances ingested without the knowledge of the victim. It did not include victims aware of their consumption, i.e., in cases of substance consumption under threat or voluntary consumption of drugs or nontherapeutic substances, which may have led to the same clinical condition as that induced by products used for CS (sedation, judgment impairment, amnesia...) and potentiated the effects of others PAS [30]. This is another aspect of drug-facilitated crime and is mostly concerned by the voluntary alcohol consumption which represents a great problem. Alcohol drinking and the use of other PAS make the victim vulnerable to assault [6].

Another form of CS is the use of drugs under duress of the assailant which is used, in this case, physical strength or weapon. This kind of assault must be integrated in the CS context because PAS is chosen by the assailant for this purpose [26, 31].

This study was not designed to estimate the prevalence of drug use and of CS among the victims of crimes such as rape, as only victims of ascertained CS were included in this study. Because these cases were reported in a voluntary way, the real frequency remains underestimated.

Conclusion

The results of this 4-year national survey show that CS is not an anecdotal phenomenon in France. It is even probably underestimated as victims of crimes such as rape are often reluctant to register a complaint and as biological sample analysis may not be contributory due to the delay in collection or to analytical difficulties surrounding determination of several substances possibly involved in CS. Information of both health professionals and of forensic structures workers about the best way to manage timely the suspected victims of chemical submission is essential to increase the recognition of such criminal actions. Education of the general population about the risk, with campaigns such as that called “watch your drink” is very important [32]. In this perspective, some night clubs have already adopted preventive measures such as protection of glasses with lids called “Bouchon anti-produits stupéfiants” (“antinarcotic cap”; BAPS Project Le Bouchon Anti Porduit Stupéfiant contre le GHB la drogue du violeur. <http://baps.cnc-com.com/php/>). Currently, for AFSSAPS, development of new dosage forms of the drugs commonly involved, in order to make them recognizable by the potential victims, is the main project in the course of achieving [21].

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