European Review for Medical and Pharmacological Sciences 2016; 20: 1174-1179

Deliberate drug poisonings admitted to an emergency department in Paris area – a descriptive study and assessment of risk factors for intensive care admission

S. BEAUNE[1,2,3,4], P. JUVIN[5], A. BEAUCHET[6], E. CASALINO[7], B. MEGARBANE[1,2,3,8]

[1]Inserm, U1144, Paris, France
[2]Université Paris Descartes, UMR-S 1144, Paris, France
[3]Université Paris Diderot, UMR-S 1144, Paris, France
[4]Assistance Publique, Hôpitaux de Paris, Hôpital Ambroise Paré, Service d'Accueil des Urgences, Boulogne, France
[5]Assistance Publique, Hôpitaux de Paris, Hôpital Georges Pompidou, Service d'Accueil des Urgences, Paris, France
[6]Assistance Publique, Hôpitaux de Paris, Hôpital Ambroise Paré, Unité de Recherche Clinique, Boulogne, France
[7]Assistance Publique, Hôpitaux de Paris, Hôpital Bichat, Service d'Accueil des Urgences, Paris, France
[8]Assistance Publique, Hôpitaux de Paris, Hôpital Lariboisière, Réanimation Médicale et Toxicologique, Paris, France

Abstract. – OBJECTIVE: Each year, approximately 165,000 poisonings are managed in the emergency departments (ED) in France. We performed a descriptive analysis of self-poisoned patients admitted to a university hospital ED in the Paris metropolitan area (France) aimed at investigating their outcome and the risk factors for transfer to the intensive care unit (ICU).

PATIENTS AND METHODS: We retrospectively reviewed patients' records and performed multivariate logistic regression analysis to identify risk factors for ICU admission.

RESULTS: During 4 years, 882 self-poisoned patients (median age, 38 years [IQR, 26-47]; sex-ratio, 1M/3F) were admitted to the ED, representing 0.7% of all referred patients. Poisonings mainly resulted from multidrug exposures (53%), including benzodiazepines (78%), serotonin reuptake inhibitors (17%), acetaminophen (13%), antipsychotics (9.5%), imidazopyridines (9.5%), antihypertensive drugs (3%), and polycyclic antidepressants (1.3%). Ethanol was involved in 20% of the exposures. Patients were briefly (<24h) monitored in the ED (55%), transferred to the psychiatric department (30%), medical ward (2%) or ICU (6%), and took an irregular discharge (7%). Among the patients transferred to the ICU, 25% were mechanically ventilated and only one died. Risk factors for ICU admission included antihypertensive (Odds ratio (OR), 40.6; 95%-confidence interval (CI), 7.5-221.9) or antipsychotic drug ingestion (OR, 5.3; CI, 2.0-14.4), male gender (OR, 3.3; CI, 1.30-8.8), and consciousness impairment (OR, 2.1; CI, 1.8-2.5 per point lost in Glasgow coma score).

CONCLUSIONS: Deliberate drug exposure represents a frequent cause of ED admission. Psychotropic drugs are most commonly involved. Transfer to the ICU is rare and predicted by male gender, drug class, and coma depth.

Key words:
Emergency department, Intensive care unit, Poisoning, Psychotropic drug, Risk factor

Introduction

According to the World Health Organization, each year about one million people die by suicide worldwide, representing around half of all violent deaths[1]. Poisoning is the third most common method of completed suicide (approximately 14% of cases), behind firearms (38%) and hanging (29%)[2]. However, attempted suicides by deliberate drug exposure are approximately 20-fold more frequent than completed suicides[3], with a rising incidence during the past decade[4]. In France, about 6% of the population has declared that they have attempted suicide at least once during their life time.[5]

Based on the annual report of the American Association of Poison Centers[6], 601,642 patients were managed in healthcare facilities in 2013 af-

Corresponding Author: Bruno Mégarbane, MD, Ph.D; e-mail: bruno-megarbane@wanadoo.fr

ter a toxic exposure. About 700,000 yearly emergency department (ED) visits have been related to deliberate drug exposures, based on the US Nationwide Emergency Department Sample, one of the Health Care Utilization Project data sets from the Agency for Healthcare Research and Quality, resulting in a more than 1 billion dollar expenditure[7]. In France, approximately 165,000 poisoned patients are admitted each year to the ED, representing ~1% of all ED admissions[5]. Interestingly, ED management of deliberate self-poisoned patients has been estimated at about $ 1,160 per patient in a Belgian study[8].

Recent data on self-poisonings admitted to the ED are scarce, but modifications in drug prescriptions are very likely to alter the prevalence of drugs involved in exposures, as has recently been shown with the reduction in fatal poisonings attributed to propoxyphene in the UK following its withdrawal from the market, without apparent significant increase in deaths involving other analgesics[9]. Additionally, about one ninth of self-poisoned patients are transferred to the intensive care unit (ICU)[6]; however, this is often based on debated and non-validated criteria. Thus, we designed the following observational study aimed at: 1. Describing self-poisoned patients admitted to a French university hospital ED; 2. Reporting ED management and outcome; and 3. Evaluating risk factors for ICU transfer.

Patients and Methods

Study Population

We conducted an observational study including all patients deliberately exposed to drugs who were admitted to the ED in a university hospital in the Paris metropolitan area, from January 2009 to December 2012. Our 460-bed hospital is located in an area serving about 255,000 people, with an ED providing care to 30,000 patients per year. This study was approved by our institutional review board.

Patients selected consisted of those encoded with a final diagnosis of "deliberate drug exposure" using the International Statistical Classification of Diseases and Related Health Problems, ICD-10, with the following categories: T36 to T50 (exposure and poisoning with drugs, pharmaceuticals and biological substances) and X60-X84 (intentional self-harm). Patients were included, independent of the available toxicological analysis, which was performed at the convenience of the physicians in charge. Patients admitted for unintentional drug exposure were excluded. The relevant information from the anonymized electronic medical records was extracted and entered into a data base (Microsoft Excel; Microsoft, Redmond, WA, USA). Data including demographics, medical history, the presumed ingested drugs and their respective doses, physical examination, laboratory testing, electrocardiogram findings, imaging, treatment, outcome, and final diagnosis were collected from patients' records using Urqual medical software (Mc Kesson, France). The presumed ingested doses of benzodiazepines, imidazopyrine-type hypnotic drugs and antipsychotic drugs were harmonized using the dose-equivalence between drugs among each class according to published tables[10,11].

Statistical Analysis

Quantitative data are expressed as median [25-75-percentiles] and qualitative data as percentage. Patients were split into two groups according to their requirement for ICU. Comparisons between the two groups were performed using Chi-2 and Man-Whitney tests, as appropriate. Statistically significant variables at a 10%-threshold in the univariate analysis were introduced into the stepwise multivariate logistic regression model to select independent predictive factors for ICU admission. Adjusted odds-ratios (OR) with their 95%-confidence intervals (CI) were determined. Statistical analysis was performed using SPSS v.19 (SSPS Inc., Chicago, IL, USA). p values < 0.05 were considered significant.

Results

During this 4-year study, 882 self-poisoned patients were admitted to our ED, representing 0.7% of all ED admissions. Sixty-seven patients (7.5%) were admitted at least twice over the study period. Patient characteristics, presentation and management are shown in Table I. Patients had a previous history of psychiatric disorders (74%) and were treated with psychotropic drugs (69%). Exposures involved at least two (52%) and three (28%) drugs (Table II). Time interval between ingestion and ED presentation was 3 h[2-6].

Based on vital parameters, patients presented significant consciousness impairment (Glasgow coma score ≤ 12, 12%), hypotension (systolic

Table I. Patient demographics, presentation on admission to the emergency department (ED), and management. Data are shown in the whole patient population as well as in the two subgroups according to the transfer or not to the intensive care unit (ICU).

	All patients (N=882)	No ICU transfer (N=832)	ICU transfer (N=50)	*p*-value
M/F sex-ratio (%)	20	20	32	0.05
Age (years)	37 [26-48][a]	38 [27-48]	41 [27-50]	0.2
Past psychiatric disorders (%)	75	74	84	0.1
Time elapsed after ingestion until ED presentation (h)	3 [2-6]	3 [2-6]	3 [2-6]	0.3
Glasgow coma score	15 [14-15]	15 [14-15]	9 [7-11]	< 0.0001
≤ 12 (%)	12	8	86	< 0.0001
Onset of seizures (%)	0.2	0	4	0.03
Heart rate (/min)	86 [75-99]	86 [75-98]	85 [71-105]	0.7
Systolic blood pressure (mmHg)				
≤ 100 mmHg (%)	115 [105-126]	115 [105-125]	121 [106-144]	0.1
	14	14	14	0.9
Diastolic blood pressure (mmHg)	75 [68-82]	75 [68-82]	76 [73-85]	0.2
≤ 60 mmHg (%)	10	10	12	0.7
Temperature	36.7 [36.3-37.0]	36.7 [36.2-36.8.0]	36.7 [36.3-37.0]	0.1
SpO_2 (%)	98 [96-99]	98 [97-99]	96 [94-98]	0.1
≤ 95% (%)	7	7	12	0.2
Blood glucose (mmol/l)	5.3 [4.8-5.8]	5.2 [4.5-5.8]	5.4 [4.7-5.9]	0.3
Electrocardiogram done (%)	87	88	82	0.3
Toxicological analysis in blood				
Acetaminophen (%)	11	11	12	0.81
Psychoactive drugs screening (%)	10	8	36	**0.001**
Ethanol (%)	20.4	19	44	**0.0001**
Salicylate (%)	0.2	0.2	0	1
Lithium (%)	0.2	0	4	1
Patient management				
Antidotes (%)	11	9	32	0.01
Activated charcoal (%)	2	2	0	1
Gastric lavage (%)	0.2	0.2	0	1
Oxygen (%)	7	4	48	0.001
Fluid replacement (%)[b]	3	2	12	0.005
Vasopressors (%)	0.2	0	4	0.003
Mechanical ventilation (%)	10	0	20	0.0001
Hemodialysis (%)	2	0	4	0.003

[a]median [25-75 percentiles];
[b]defined as infusion of at least 500 ml of crystalloids or colloids in the presence of hypotension.

blood pressure ≤ 100 mmHg, 14%), and oxygen desaturation (SpO_2 ≤ 95%, 7%). Only two patients, one poisoned with venlafaxine (presumed ingested dose: 1.5 g) and the second poisoned with citalopram (presumed ingested dose: 600 mg), developed seizures. Electrocardiogram, performed in 87% of the cases, showed sinus tachycardia (28%), atrial fibrillation (0.2%), and slight QT prolongation (0.1%). Antidotes administered in the ED included flumazenil (6%), N-acetylcysteine (5%), and naloxone (0.6%).

Patients were monitored for a short time (< 24h) in the ED (55%), transferred to the psychiatry department (30%), medical ward (2%) or ICU (6%), and discharged against medical advice (7%). One verapamil-poisoned patient (presumed ingested dose: 3,600 mg) died in the ED due to a sudden cardiac arrest on admission.

Univariate comparison of the patients according to requirement for ICU is presented in table II. Based on a multivariate analysis, four independent variables were predictive of ICU admission (Table III): ingestion of an antihypertensive drug (OR, 40.6; CI, 7.5-221.9); ingestion of an antipsychotic drug (OR, 5.3; CI, 2.0-14.4), male gender (OR, 3.3; CI, 1.30-8.8), and consciousness impairment (OR, 2.1; CI, 1.8-2.5 per point lost in Glasgow coma score).

Table II. Drugs involved in the 882 deliberate exposures (and their equivalent doses).

Benzodiazepines	78 %
Ingested equivalent diazepam dose	150 mg [70-300][a]
Serotonin re-uptake inhibitors	17 %
Acetaminophen	13 %
Ingested dose	4,000 mg [2,000-8,000]
Imidazopyrine-type hypnotics	10 %
Ingested equivalent zolpidem dose	100 mg [50-280]
Antipsychotic drugs	10 %
Ingested equivalent chlorpromazine dose	1000 mg [200-2,000]
Non-steroidal anti-inflammatory drugs	8 %
Antihypertensive drugs	3 %
Tramadol	3 %
Ingested dose	300 mg [113-788]
Other opioids	2 %
Polycyclic antidepressant drugs	1.3 %
Meprobamate	1 %
Oral anti-diabetics drugs	1 %

[a]median [25-75 percentiles]

Discussion

This observational study provides detailed insight into ED admission in relation to self-poisoning in the Paris area. Deliberate drug exposures represented 0.7% of all ED admissions, which was consistent with previously published data[3,8,12-14]. Consistently, our study population was comparable to previous series[3,8,12-14], regarding age, female predominance, and ~3h time lapse between ingestion and ED presentation. Interestingly, this time was consistent with the threshold (time < 2h) reported to be a risk factor for ICU admission[15].

Multidrug poisoning is an increasing concern[6,7,16], representing ~50% of the cases in our series and at least in part explained by the high rate of self-poisoned patients with past psychiatric disorders (74%). Interestingly, it was previously shown that psychiatric patients have a greater number of prescribed drugs in comparison to the general population[17], and thus are more at risk for multidrug exposure, as patients usually tend to ingest their own medications in attempting suicide[18].

Regarding the presumed ingested drugs, benzodiazepines represented the most common class of pharmaceuticals, as reported in France[19] and Belgium[8], contrasting with the US[7] and UK[12,13], where analgesics and antidepressants are responsible for the majority of ED visits. Serotonin reuptake inhibitors ranked in the second position, in contrast to previous French studies[19,20], suggesting a growing role in drug exposures as elsewhere in the western countries and thus calling for increased awareness among emergency physicians to improve diagnosis and management. As expected, acetaminophen exposures ranked third but were less frequent in our series than in the UK series[12,13], but were, however, consistent with other French and Belgian series[8,19,20], highlighting regional specificities in Europe in the drugs involved in self-poisoning episodes presenting to the ED. In our study, the median acetaminophen dose was under or near its toxic dose, supporting the benefits of a more restrictive legislation in pack size and conditions of acetaminophen sale, as shown in the UK[21]. Finally, antipsychotic drugs ranked fourth due to increasing prescriptions by psychiatrists, as previously reported in France[20].

Gastrointestinal decontamination was performed in < 2% of the patients, consistent with the time elapsed after ingestion before ED presentation

Table III. Predictive factors for transfer of poisoned patients to the intensive care unit (ICU) using a logistic regression analysis.

	All patients (N=882)	No ICU transfer (N=832)	ICU transfer (N=50)	Adjusted Odds ratio [95%-confidence interval]	*p*-value
Exposure to antihypertensive drugs	3 %	2 %	26 %	40.6 [7.5 - 221.9]	< 0.0001
Exposure to antipsychotic drugs	10 %	8 %	40 %	5.3 [2.0 - 14.4]	0.001
Male gender	20 %	20 %	32 %	3.3 [1.3 - 8.8]	0.013
Glasgow Coma Scale (per point lost)	15 [14-15][a]	15 [14-15]	9 [7-11]	2.1 [1.8 - 2.5]	< 0.0001

[a]median [25-75 percentiles]

and in agreement with the current international and national recommendations[22-24]. Accordingly, only 12% of our patients were admitted to the ED in the first hour after drug exposure. However, our findings contrasted with the Belgian study reporting activated charcoal administration in 70% of the patients but were more in accordance with the Scottish study, where only 1.5% received activated charcoal and no gastric lavage was performed[11].

In our work, most of the patients (>80%) had stable vital signs on ED presentation; only 5% of them were transferred to the ICU, similar to previous European series[25,26]. We showed that transfer of self-poisoned patients from the ED to the ICU is predicted by the ingested drug class, the male gender, and the depth of unconsciousness. Neither the heart rate nor the blood pressure nor oxygen saturation was associated with ICU admission. Not surprisingly, respiratory rate was missing in more than 90% of the charts, despite its importance for specific poisonings[27]. The life-threatening consequences of overdoses involving antihypertensive and antiarrhythmic drugs are well-established; experts recommend that symptomatic patients exposed to such drugs should be admitted to the ICU[15,24]. Overdoses with antipsychotics may also result not only in significant neurological depression, as observed in our study, but also in possible cardiovascular events[28], justifying ICU referral. The association between male gender and ICU admission seems less clear; it may reflect the fact that self-poisoned men are more likely to be admitted with greater severity of poisoning in the ED since, in comparison to women, they more frequently complete suicide, even in self-poisonings[29]. Finally, despite persistent debates on its usefulness in indicating the need for tracheal intubation in poisoned patients admitted to the ED[30,31], the Glasgow coma score was the only clinical finding associated with ICU admission in our series, mainly due to the high prevalence of exposures to psychotropic drugs. In one previous study, coma upon ED presentation (OR=15.8, CI 4.9-50.7) was shown to be predictive of ICU admission after deliberate drug overdose[15]. In a second study, the Glasgow coma scale was the only clinical feature associated with ICU transfer (OR, 1.57; CI, 1.44-1.70 for each point loss) of deliberate drug poisonings with minor symptoms on ED admission[25].

Limitations

Our study presents some significant limitations due to its methodology based on the retrospective evaluation of patients' charts. However, although the data base has been accessed retrospectively, the data capture from patient's charts was prospective using a robust system by trained dedicated staff. Self-exposures were based on the ingested toxicants reported by the patient himself and not systematically confirmed by toxicological analysis, as left at the appreciation of the physicians in charge.

Conclusions

Deliberate drug exposure represents a frequent cause of ED admission. Psychotropic drugs are most commonly involved. Transfer to ICU remains rare and predicted by male gender, drug class, and coma depth. A large prospective multicenter study is still mandatory to confirm our findings, in order to validate prognostic scores and improve specific management strategies for self-poisoned patients in the ED.

Acknowledgment
The authors are thankful for financial support from Taisei Kogyo Co., Ltd. (CDE26014). The authors also thank Natural Product Industry of Tsukuba Co., Ltd. for providing the plant material and thank Professor Ende Liu for identifying the plant material.

Conflict of Interests
The authors declare no conflicts of interest.

References

1. WHO. SUPRE Prevention of suicidal behaviours: a task for all. Available at http://www.who.int/mental_health/prevention/suicide/supresuicideprevent/en/. Accessed on October 29th, 2015.
2. Miller M, Azrael D, Hemenway D. The epidemiology of case fatality rates for suicide in the northeast. Ann Emerg Med 2004; 43: 723-730.
3. Ting SA, Sullivan AF, Boudreaux ED, Miller I, Camargo CA Jr. Trends in US emergency department visits for attempted suicide and self-inflicted injury, 1993-2008. Gen Hosp Psychiatry 2012; 34: 557-565.
4. Prosser JM, Perrone J, Pines JM. The epidemiology of intentional non-fatal self-harm poisoning in the United States: 2001-2004. J Med Toxicol 2007; 3: 20-24.
5. [Prise en charge des suicidants]. Available at http://www.clientsinterface-messidor.com/pdf/Suicide-Jaman2008.pdf. Accessed on October 29th, 2015.

6. Mowry JB, Spyker DA, Cantilena LR Jr, McMillan N, Ford M. 2013 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 31st Annual Report. Clin Toxicol (Phila) 2014; 52: 1032-1283.
7. Xiang Y, Zhao W, Xiang H, Smith GA. ED visits for drug-related poisoning in the United States, 2007. Am J Emerg Med 2012; 30: 293-301.
8. Hendrix L, Verelst S, Desruelles D, Gillet JB. Deliberate self-poisoning: characteristics of patients and impact on the emergency department of a large university hospital. Emerg Med J 2013; 30: e9.
9. Hawton K, Bergen H, Simkin S, Wells C, Kapur N, Gunnell D. Six-year follow-up of impact of coproxamol withdrawal in England and Wales on prescribing and deaths: time-series study. PLoS Med 2012; 9: e1001213.
10. Ashton CH. Benzodiazepines: How they work and how to withdraw. Drug and dependence. London: Harwood Academic Publishers, 2002.
11. Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. J Clin Psychiatry 2003; 64: 663-667.
12. Cook R, Allcock R, Johnston M. Self-poisoning: current trends and practice in a U.K. teaching hospital. Clin Med 2008; 8: 37-40.
13. Prescott K, Stratton R, Freyer A, Hall I, Le Jeune I. Detailed analyses of self-poisoning episodes presenting to a large regional teaching hospital in the UK. Br J Clin Pharmacol 2009; 68: 260-268.
14. Doshi A, Boudreaux ED, Wang N, Pelletier AJ, Camargo CA Jr. National study of US emergency department visits for attempted suicide and self-inflicted injury, 1997-2001. Ann Emerg Med 2005; 46: 369-375.
15. Novack V, Jotkowitz A, Delgado J, Novack L, Elbaz G, Shleyfer E, Barski L, Porath A. General characteristics of hospitalized patients after deliberate self-poisoning and risk factors for intensive care admission. Eur J Intern Med 2006; 17: 485-489.
16. Bateman DN. The epidemiology of poisoning. Medicine (Baltimore) 2007; 35: 537-539.
17. Gjelsvik B, Heyerdahl F, Hawton K. Prescribed medication availability and deliberate self-poisoning: a longitudinal study. J Clin Psychiatry 2012; 73: e548-554.
18. Tournier M, Grolleau A, Cougnard A, Molimard M, Verdoux H. Factors associated with choice of psychotropic drugs used for intentional drug overdose. Eur Arch Psychiatry Clin Neurosci 2009; 259: 86-91.
19. Staikowsky F, Theil F, Mercadier P, Candella S, Benais JP. Change in profile of acute self-drug poisonings over a 10-year period. Hum Exp Toxicol 2004; 23: 507-511.
20. Adnet F, Atout S, Galinski M, Lapostolle F. [Évolution des intoxications médicamenteuses volontaires en France]. Réanimation 2005; 14: 721-726.
21. Hawton K, Simkin S, Deeks J, Cooper J, Johnston A, Waters K, Arundel M, Bernal W, Gunson B, Hudson M, Suri D, Simpson K. UK legislation on analgesic packs: before and after study of long term effect on poisonings. Br Med J 2004; 329: 1076-1079.
22. Benson BE, Hoppu K, Troutman WG, Bedry R, Erdman A, Höjer J, Mégarbane B. Position paper update: gastric lavage for gastrointestinal decontamination. Clin Toxicol (Phila) 2013; 51: 140-146.
23. Chyka PA, Seger D, Krenzelok EP, Vale JA; American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position paper: single-dose activated charcoal. Clin Toxicol (Phila) 2005; 43: 61-87
24. Mégarbane B, Donetti L, Blanc T, Chéron G, Jacobs F, Groupe d'experts de la SRLF. [Intoxications graves par médicaments et substances illicites en réanimation]. Réanimation 2006; 15: 332-342.
25. Maignan M, Pommier P, Clot S, Saviuc P, Debaty G, Briot R Carpentier F, Danel V. Deliberate drug poisoning with slight symptoms on admission: are there predictive factors for intensive care unit referral? A three-year retrospective study. Basic Clin Pharmacol Toxicol 2014; 114: 281-287.
26. Schwake L, Wollenschläger I, Stremmel W, Encke J. Adverse drug reactions and deliberate self-poisoning as cause of admission to the intensive care unit: a 1-year prospective observational cohort study. Intensive Care Med 2009; 35: 266-274.
27. Sungur M, Güven M. Intensive care management of organophosphate insecticide poisoning. Crit Care 2001; 5: 211-215.
28. Ciranni MA, Kearney TE, Olson KR. Comparing acute toxicity of first- and second-generation antipsychotic drugs: a 10-year, retrospective cohort study. J Clin Psychiatry 2009; 70: 122-129.
29. Camidge DR, Wood RJ, Bateman DN. The epidemiology of self-poisoning in the UK. Br J Clin Pharmacol 2003; 56: 613-619.
30. Duncan R, Thakore S. Decreased Glasgow Coma Scale score does not mandate endotracheal intubation in the emergency department. J Emerg Med 2009; 37: 451-455.
31. Chan B, Gaudry P, Grattan-Smith TM, McNeil R. The use of Glasgow Coma Scale in poisoning. J Emerg Med 1993; 11: 579-582.