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Factors associated with choice of psychotropic drugs used for intentional drug overdose

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■ **Abstract** *Introduction* Knowledge of the factors influencing the choice of drugs used for intentional drug overdose (IDO) may allow the reduction of IDO lethality. Objectives To assess with which frequency subjects with intentional overdose of psychotropic drugs ingest their own psychotropic drug treatment, and whether prescription of a drug may be a factor influencing the choice of drugs used for the IDO. Methods Demographic characteristics, psychiatric history, and currently prescribed psychotropic drug treatment were collected for all the patients (n = 1,654) admitted to an emergency department (ED) for IDO with psychotropic drugs (anxiolytics, hypnotics, antidepressants, neuroleptics and mood stabilizers) over a period of 18 months. Drugs ingested for the IDO were compared in subjects who had ingested at least one psychotropic drug that was prescribed for them and subjects who had ingested psychotropic drugs not prescribed for them using multivariate logistic regression. Results Two-thirds of the patients ingested during the IDO at least one of their own prescribed psychotropic drugs. Compared with the subjects who had ingested psychotropic drugs not prescribed for them, they were more likely to have a history of psychiatric hospitalization (OR 4.2; 95%CI 3.1-5.5), of being a psychiatric outpatient (OR 3.9; 95%CI 3.0-5.1), of parasuicide (OR 2.5; 95%CI 1.9-3.3) and a serious IDO (OR 2; 95%CI 1.4-2.9). Independently from age and psychiatric hospi-

psychotics (OR 2.9; 95%CI 1.7–4.8) and mood stabilizers (OR 4.1; 95%CI 1.6–10.7). No association was found with prescription for overdose of hypnotic (OR 1.1; 95%CI 0.8–1.5), anxiolytic (OR 1.2; 95%CI 0.9–1.7) or paracetamol (OR 1.0; 95%CI 0.5–2.1). Conclusion Prescription of the psychotropic drugs plays an important role in the choice of the drugs ingested for the IDO. It might make potentially "dangerous" drugs available for the patient. Physicians have always to balance the benefit of the treatment against the risk of drug overdose.

talization history, they ingested during the IDO more

often antidepressants (OR 4.4; 95%CI 3.0-6.4), anti-

■ **Key words** parasuicide · overdose · psychotropic drugs · prescription

Introduction

Parasuicide is frequent in the general population, particularly among adolescents and young adults [18]. Intentional drug overdose (IDO), the most common method of parasuicide in people who present to hospital [1, 10, 22], is defined as "an act with nonfatal outcome in which an individual deliberately ingests a substance in excess of the prescribed or generally recognized therapeutic dosage and which is aimed at realizing changes which the subject desired via the actual or expected physical consequences" [25]. Psychotropic drugs are, with analgesics, the drugs most frequently involved in IDO [1, 4, 19, 24, 27] and the drugs responsible for the largest number of deaths after an overdose [20]. Knowledge of the factors influencing the choice of drugs used for IDO may allow the reduction of IDO lethality, for example by reducing availability and avoiding household stocks of dangerous drugs [10, 27].

For psychotropic drugs as for analgesics, changes in rates of IDO using a given drug correspond

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with changes in prescription rates of this drug in a given country [7, 12, 14, 27]. Therefore, it is usually considered that a patient who IDOs ingests those prescribed to him/her. However, compared to prescription data, psychotropic drugs such as antidepressants, antipsychotics, lithium or benzodiazepines are overrepresented in IDOs [5]. Moreover, subjects under 45 years have the highest risk for IDO while they are the least likely to be prescribed psychotropic drugs [4]. Hence, availability of the drug may not be the single factor motivating the choice of the drug used for IDO. Very few studies investigated if subjects with IDO ingested their own drug treatment [1, 8]. No study has compared the subjects ingesting their own prescribed drug treatment to those ingesting drugs not prescribed for them.

The objectives of the present study were to assess with which frequency subjects with intentional overdose of psychotropic drugs ingest their own psychotropic drug treatment, whether subjects who had ingested psychotropic drugs not prescribed for them differ from subjects who had ingested at least one of their own prescribed psychotropic drugs, and whether prescription of a drug may be a factor influencing the choice of drugs used for the IDO.

Materials and methods

Study population

The method has previously been presented in part [30–32]. All the patients consecutively admitted for IDO to the emergency department (ED) of the University General Hospitals in Bordeaux over a period of 18 months (July 2001–December 2002) were recruited if they fulfilled the following criteria: (1) IDO defined as a substance ingestion in excess of the prescribed or generally recognized therapeutic dosage; (2) directly admitted to the ED after IDO, i.e. not referred by other hospitals for complicated IDO. Only the first admission was considered for subjects hospitalized several times for IDO over the study period. For the present study, only subjects who had ingested psychotropic drugs for the IDO were included.

■ Data collection

Data were drawn from medical records using information collected in routine clinical practice by the staff of the ED. A trained research assistant filled in a standardized form concerning the following: (1) demographic characteristics; (2) characteristics of the IDO: ingested drugs, ingestion of alcohol, and medical management over the hospitalization stay; (3) psychiatric history: prior parasuicide, psychiatric hospitalization, current psychiatric follow-up; (4) currently prescribed psychotropic drug treatment.

Patients' current psychotropic drug treatment and drugs ingested during the IDO were noted from medical charts using the information obtained and recorded during the hospital stay by the staff of the ED, including liaison psychiatrists. The staff did not receive any specific instructions about collecting the information. Subjects may have been questioned about their drug treatment and the drugs ingested during the IDO; this information may also have been obtained from other sources such as the general practitioner, firemen, relatives or friends. No information was collected on dosages. The psychotropic drugs, including anxiolytics, hypnotics, antidepressants, neuroleptics and mood stabilizers, were catego-

rized using the anatomical therapeutic chemical (ATC) classification [34]. However, as the ATC classification gathers together all the antipsychotic medications, the EphMRA classification [11] was used in order to distinguish between first- and second-generation antipsychotics. Although the study was focused on psychotropic drugs, we also investigated characteristics associated with ingestion of paracetamol, as this drug is often involved in IDO in many countries [12, 22, 23] and widely available in France. Drugs defined as "dangerous" were those independently associated with serious IDO in the present sample: tricyclic antidepressant (TCA), serotonin selective reuptake inhibitor (SSRI), lithium, anticonvulsant mood stabilizer, first-generation antipsychotic, carbamate [29]; a serious IDO being a priori defined as IDO associated with at least one of the following events: death, ED hospitalization longer than 48 h, respiratory support, use of vasopressive drugs, cardiac massage or dialysis [30].

The study conformed to the French bioethics and clinical research and data protection legislation. All data were de-identified. No informed consent was requested as the data were collected during the routine IDO management process, and no supplementary medical procedure was mandated by the study.

Statistical analysis

Statistical analyses were conducted using STATA 9 software [28]. Chi-square test and Student's t test were used to compare the characteristics of subjects with and without missing data. Univariate logistic regression was used to compare subjects who had ingested at least one psychotropic drug that was prescribed for them to subjects who had ingested psychotropic drugs not prescribed for them (reference population). Then, drugs ingested for the IDO were compared in both groups of subjects using multivariate logistic regression after adjustment for age and history of psychiatric hospitalization; the later characteristic being used as a proxy for seriousness of the psychiatric disorder.

Results

Over the study period, 1,974 subjects were admitted at least once for IDO. Among them, 1,654 (83.8%) overdosed psychotropic drugs. Information was available with respect to prescribed treatment for 1,321 subjects (79.9%) who were the study population. Compared to subjects without missing data, subjects with missing data had more frequently a parasuicide history (n = 131,71.2% vs. n = 654,63.4%; $\chi^2 = 4.2, P = 0.04$) and less frequently overdosed mood stabilizer (n = 11,3.3% vs. n = 85,6.4%; $\chi^2 = 4.8, P = 0.03$). They did not differ regarding the other demographic or clinical characteristics.

Among subjects included in the study, 865 (65.5%) ingested at least one of their own prescribed psychotropic medications for the IDO. The univariate comparison of subjects who had ingested psychotropic drugs that were not prescribed for them to those who had ingested at least one of their own prescribed psychotropic drugs is given in Table 1. Subjects who had overdosed their own psychotropic drug treatment were slightly older. There was no other difference between the two groups with respect to demographic characteristics, in particular regarding gender. Compared to the subjects who had ingested psychotropic drugs that were not prescribed for them, subjects who

Table 1 Comparison of the subjects who had ingested at least one of their own prescribed psychotropic drugs and those who had ingested psychotropic drugs not prescribed for them

	Ingestion of at least one prescribed psychotropic drugs ($n = 865$)			Ingestion of not prescribed psychotropic drugs ($n = 456$)			Mann Whitney <i>U</i> test		Р
	Mean	SD		Mean		SD			
Age $(n = 1,320)^{a,c}$	38.5	14.4		34.9		14.0	z = -4.6		<0.0001
		Ingestion of at least one prescribed psycho- tropic drugs (n = 865)		Ingestion of prescribed p		psychotropic	OR	95CI%	Р
		Number	%		Number	%			
Gender, female $(n = 1,320)^a$		609	70.4		313	68.8	1.1	0.8-1.4	0.5
Married $(n = 1,131)^{a}$		318	43.6		174	43.4	1.0	0.8-1.3	0.9
Living alone $(n = 837)^a$		158	28.8		69	24.0	1.3	0.9-1.8	0.1
Employedb (n = 680)a		282	64.5		172	70.8	0.8	0.5–1.1	0.1
Psychiatric hospitalization $(n = 943)^a$		391	64.8		104	30.6	4.2	3.1–5.5	< 0.0001
Psychiatric outpatient $(n = 1,119)^a$		468	64.8		127	32.0	3.9	3.0-5.1	< 0.0001
Parasuicide history $(n = 1,032)^a$		469	71.3		185	49.5	2.5	1.9–3.3	< 0.0001
Alcohol during IDO $(n = 1,319)^a$		279	32.3		142	31.2	1.1	0.8-1.3	0.7
Serious ^d IDO $(n = 1,321)^a$		134	15.5		38	8.3	2.0	1.4-2.9	< 0.0001

^aNumber of subjects for whom information was available is in brackets

overdosed their own treatment had more frequently a history of parasuicide, of psychiatric hospitalization and a current psychiatric follow-up. They were twice more likely to be currently admitted for a serious IDO. Drug classes ingested for the IDO are detailed in Table 2 for both groups of subjects. Overall, benzo-diazepine or benzodiazepine-like drugs (hypnotic or anxiolytic combined together) were the most fre-

Table 2 Comparison of the drugs ingested during the IDO by the subjects who had ingested at least one of their own prescribed psychotropic drugs and those who had ingested psychotropic drugs not prescribed for them

	Ingestion of at least one prescribed psychotropic drugs (n = 865)		Ingestion of not prescribed psychotropic drugs ($n = 456$)		Adjusted OR ^a		
	N	%	N	%	OR	95%CI	Р
Dangerous drugs during IDO	438	50.8	99	21.7	3.5	2.6–4.9	<0.0001
At least one hypnotic	244	28.2	119	26.1	1.1	0.8-1.5	0.6
Benzodiazepine	207	23.9	103	22.6	1.1	0.8-1.5	0.6
Other hypnotics	40	4.6	14	3.1	1.4	0.6-2.9	0.4
At least one anxiolytic	678	78.4	350	76.8	1.2	0.9-1.7	0.2
Benzodiazepine	611	70.6	317	69.5	1.1	0.8-1.6	0.4
Carbamate	93	10.8	27	5.9	1.5	0.9-2.4	0.2
Other anxiolytics	51	5.9	21	4.6	1.9	1.0-3.6	0.04
At least one antidepressant	311	36.0	62	13.6	4.4	3.0-6.4	< 0.0001
SSRI	200	23.1	38	8.3	4.6	2.9-7.2	< 0.0001
Tricyclic	42	4.9	8	1.8	2.3	0.9-6.0	0.08
Other antidepressants	70	8.1	17	3.7	2.1	1.0-4.1	0.04
At least one antipsychotic	175	20.2	27	5.9	2.9	1.7-4.8	< 0.0001
Second generation	46	5.3	3	0.7	3.9	1.2-12.9	0.03
First generation	131	15.1	23	5.0	2.6	1.5-4.5	0.001
At least one mood stabilizer	78	9.0	7	1.5	4.1	1.6-10.7	0.003
Lithium	17	2.0	1	0.2	3.8	0.5-29.5	0.2
Anticonvulsants	62	7.2	6	1.3	4.1	1.4-11.9	0.009
Paracetamol	30	3.5	21	4.6	1.0	0.5-2.1	0.9

SSRI Selective serotonin reuptake inhibitor

^bIncluding students, housewives, and retired subjects

^cStandard deviation

^dAt least one event: death, ED hospitalization longer than 48 h, respiratory support, vasopressive drugs, cardiac massage or dialysis

^aAge and psychiatric hospitalization history

quently ingested (79.9% of subjects, n=1,055) without difference between the two groups [79% of subjects who had ingested their own prescribed psychotropic drugs (n=683) vs. 81.6% of subjects who had ingested psychotropic drugs that were not prescribed for them (n=372)]. A quarter of the subjects (n=121,26.5%) who had ingested psychotropic drugs that were not prescribed for them were nevertheless currently prescribed psychotropic drugs [hypnotics 14.9% (n=18); anxiolytics 15.7% (n=19); antidepressants 68.6% (n=83); antipsychotics 25.6% (n=31); mood stabilizers 19% (n=23)].

Compared to subjects ingesting drugs not prescribed for them, subjects who had ingested their own prescribed psychotropic drugs were more than three times more likely to have ingested "dangerous" drugs. In particular, they had ingested more often antidepressant, antipsychotic and mood stabilizer. Among these therapeutic classes, significant associations with adjusted ORs ranging between 2.1 and 4.6 were found for most pharmacological classes except lithium and tricyclics. No association was found with prescription for overdose of benzodiazepine or paracetamol (ORs close to one).

We assessed the association between the choice of a given psychotropic product used for IDO and its prescription for the most frequent product within each subclass: ingestion of zolpidem [101 patients who had ingested at least one of their own prescribed psychotropic drugs (11.7%) vs. 62 patients who had ingested psychotropic drugs not currently prescribed for them (13.6%); OR 0.8 (95%CI 0.5–1.3), P = 0.4], ingestion of bromazepam [230 (26.6%) vs. 163 (35.8%); OR 0.7 $(95\%CI\ 0.5-1.0)$, P = 0.03, ingestion of fluoxetine [68 (7.9%) vs. 13 (2.9%); OR 3.8 (95%CI 1.8-8.2), P = 0.001; ingestion of venlafaxine [42] (4.9%) vs. 9 (2.0%); OR 1.8 (95%CI 0.8-4.2), P = 0.2], ingestion of clomipramine [23 (2.7%) vs. 3 (0.7%); OR 2.9 (95%CI 0.8–10.7) P = 0.1], ingestion of cyamemazine [93 (10.8%) vs. 16 (3.5%); OR 2.2 (95%CI 1.2-4.1), P = 0.01, ingestion of risperidone [19 (2.2%) vs. 1 (0.2%); OR 3.7 (95%CI 0.5–29.0), P = 0.2] and ingestion of valpromide [36 (4.2%) vs. 2 (0.4%); OR 4.5 (95%CI 1.0–19.6), P = 0.04]. The most frequently prescribed product within each subclass was also always the most frequently ingested during the IDO. These results were consistent with the results found using subclasses.

Discussion

Two-thirds of the subjects ingested at least one of their own prescribed psychotropic drugs during the IDO. Compared with the subjects who had ingested psychotropic drugs not prescribed for them, they were more likely to be older, to have a history of serious psychiatric disorder and a serious IDO. Independently from age and psychiatric hospitalization history, they ingested more often antidepressants, antipsychotics and mood stabilizers.

The present study had potential methodological limitations. First, as the study was carried out in hospitalized subjects, this recruitment excluded subjects with IDO not referred to a hospital, i.e. minor or unidentified IDOs and complete suicides. This potential bias may have had an impact on the types of drugs ingested during the IDO; the subjects with minor IDO being more likely to have ingested the least dangerous drugs such as mild sedatives and the victims of suicide the most dangerous ones such as tricyclics. However, the sample was representative of subjects with IDO approachable in routine practice in an emergency department, and our main aim was not to explore the exact prevalence of psychotropic drugs used for IDO. Drugs ingested during the IDO, as well as patients' current psychotropic drug treatments, were identified through information recorded in medical charts and not using blood tests. The accuracy of the results could have been compromised by inaccurate patient statements [21], improper assessment or inaccurate recording by the emergency staff [33]. All these biases are unlikely to have had a marked impact on the comparison between the two groups of subjects, since there is little reason to suspect that they were systematically associated with whether the subject with IDO took an overdose of prescribed psychotropic drugs or not. Lastly, information was collected only on currently prescribed drugs. Thus, some subjects may have been misclassified as subjects who did not ingest drugs prescribed for them for the IDO as no information was available on medications prescribed in the past. However, this misclassification bias may have attenuated the differences between both studied groups and did not induce spurious significant associations.

What might be the reasons for choosing specific types of psychotropic drugs in the present sample? As in many studies, psychotropic drugs were the most frequently drugs involved in IDO. Benzodiazepines or benzodiazepine-related drugs were the most frequently identified, with the same frequency in subjects who had ingested their own prescribed psychotropic drugs or psychotropic drugs not prescribed to them. As benzodiazepines are very frequently prescribed in France [2], these drugs may be widely available for many people with household stocks. Thus, subjects not prescribed benzodiazepines may have easy access to these drugs if they have been prescribed for them in the past or if they were prescribed for someone else of the household. Most of the other psychotropic drugs are less frequently prescribed and less available and subjects who ingested antidepressants, antipsychotics or mood stabilizers for the IDO were more likely to be prescribed the drugs they overdosed. These findings were similar to those obtained in a Spanish sample; benzodiazepine overdose was the only one that was not influenced by prescription [1]. In the Spanish study, all subjects who overdosed antipsychotics were prescribed antipsychotics, which was the case for only two-thirds of patients who used antipsychotics for the IDO in the present study. This might reflect the differences of local prescription habits and a greater availability of antipsychotics in the present sample.

Subjects who overdosed their own prescribed psychotropic drugs were prone to use less available drugs. Overall, they were prone to use more "dangerous" drugs and, as a probable consequence, they were more likely to have taken a serious IDO. They were older and had more frequently a psychiatric history (as an inpatient, outpatient or parasuicide), i.e. presented probably with more serious psychiatric disorders. Thus, they might have chosen these drugs either because of their availability, or because they expected these drugs to be more dangerous in the context of an older age, a more serious psychiatric disorder and, maybe, a higher suicidal intent. Indeed, suicidal intent has been found to be associated with age and seriousness of psychiatric disorders [13, 26]. However, the associations between prescription and types of drugs chosen for the IDO were independent from the age and the history of psychiatric hospitalization, i.e. the seriousness of psychiatric disorder. Availability of the medication might be an important motivation for choosing it for the IDO independently of degree of suicidal intent.

Availability of the drug might not be the only factor motivating the choice of the drug. A quarter of the subjects who had ingested psychotropic drugs not prescribed for them were nevertheless currently prescribed psychotropic drugs and they have chosen not to ingest these drugs for the IDO. Moreover, paracetamol was much less frequently involved in IDO in the present French sample than in comparable sample recruited in other countries [12, 15, 16, 19, 22-24]. This low frequency contrasts with the fact that paracetamol is the most frequently prescribed analgesic in France [6] and is also available over-the-counter. The fact that pack size of paracetamol is restricted in France does not explain the low use of this drug for IDO since it does not prevent obtaining large supplies from purchasing through several outlets [15]. A study carried out in UK showed that availability of paracetamol was the most common reason for choosing it for IDO [17]. However, many users thought the drug was dangerous and sedative, because of an extensive media warning conducted in UK about paracetamol overdose. Thus, the expected effects of a drug may also play a role for choosing it for overdose purpose. The design of the present study did not allow us to explore this issue, which deserves further studies.

In conclusion, the present findings suggest that availability of the psychotropic drugs through prescription might play an important role in the choice of the drugs ingested for the IDO. Prescription makes a potentially "dangerous" drug available for the pa-

tient and sometimes his/her household. Contacts with physicians and "doctor shopping" behavior increase in the period before suicide [9]. In subjects liable to have suicidal behaviour, physicians have always to balance the benefit of the treatment against the risk of drug overdose [3, 4]. Some precautions may hence be undertaken such as prescriptions of short duration, or getting back the tablets when a treatment is stopped.

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