ORIGINAL ARTICLE

Comprehensive drug screening in decision making of patients attending the emergency department for suspected drug overdose

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Objectives: This study aimed to evaluate the usefulness of a comprehensive drug screening method as a first line diagnostic tool on clinical decision making in patients attending an emergency department for suspected drug overdose in terms of agreement between physicians on patients' disposal.

Methods: Five emergency physicians retrospectively evaluated the records of 142 adult patients, admitted to the emergency department of a community hospital for suspected drug overdose. They were asked for an expert opinion on patients' disposal at the end of the observation period, based on paired records, with/without the results of a comprehensive drug screening.

Results: In the absence of the drug screening, a very poor agreement (κ statistics) was observed between physicians. When the drug screening was available, the interobserver agreement for decision on patients' disposal increased to the fair to good range (global agreement: from 0.238 (0.019) to 0.461 (0.020) (mean(SE)); p<0.001). The agreement also increased when admission to an intensive care unit, to a general ward, and discharge from hospital were separately analysed. The availability of drug screening would have saved 21.7% of hospital admissions and 53.3% of high dependency and/or intensive care unit admissions.

Conclusion: Comprehensive drug screening adds to decision making for patients attending an emergency department for suspected drug overdose, improving agreement among physicians on patients' disposal and potentially saving hospital resources.

The initial assessment and treatment of patients attending an emergency department (ED) for suspected drug poisoning takes place in the emergency room, where the busy physicians must rapidly decide on the level of therapeutic measures and disposal. Decontamination procedures for drug overdose are recommended under specific circumstances by the American Academy of Clinical Toxicology and by the European Association of Poison Centres and Clinical Toxicology in a joint position statement,[1] but their efficacy is questioned. The most important measure is a correct management of individual patients, according to their clinical status and hospital resources.

In unstable patients, lifesaving support is mandatory, independently of laboratory results, whereas in uncomplicated, stable, slightly drowsy patients, with no specific symptoms of drug poisoning, the diagnosis may be uncertain, and there is no definite consensus on treatment and disposal.

These patients are a special challenge for the emergency physicians. A pure clinical approach, without confirmatory laboratory results, makes diagnosis and decision making highly uncertain. Some patients need only a brief period of observation in ED, while others may need care in a high dependency unit (HDU) or in intensive care unit (ICU), in relation to worsening clinical status or long acting drug overdose.

Comprehensive drug screenings have been proposed to document and confirm any acute drug overdose in patients for suspected poisoning.[2] A screening procedure is operative in our unit, permitting the determination of over 900 drugs and their metabolites in a turnaround of 20 to 60 minutes. Its usefulness has however been questioned[3]; in most cases the results do not change, the decision being mainly based on clinical parameters.[4] Drug screening, limited to life threatening drugs selected on the basis of the clinical suspect, is currently considered a cost effective diagnostic tool.[5][6]

The aim of this study was to evaluate the effects of comprehensive drug screening in decision making strategies of patients with suspected drug poisoning. In particular, we aimed to determine whether the results of such screening improved the agreement in an expert panel of emergency physicians and changed the decision on patients' disposal, potentially saving hospital resources.

METHODS

Study protocol

A panel of five physicians (A, B, C, D, E), with more than 10 years of experience in emergency medicine, was appointed to give an expert opinion on appropriateness of patient management, after reviewing the records of 142 patients who attended the ED of Forlì, Italy, for suspected intentional drug overdose. All patients had been submitted to comprehensive drug screening. The experts blindly received two datasheets for each case. One datasheet omitted the results of the comprehensive drug screening (see below), while the second, which included drug screening results, was slightly modified in terms of minor data concerning history, to make the paired datasheets unidentifiable as pertaining to the same patient. The sequence of cases was also randomly determined to exclude any identification.

The experts were asked to complete a questionnaire regarding the appropriateness of patients' disposal (discharge after three to six hours of observation, general wards admission, HDU/ICU observation).[7] Before revision, experts were also informed on the criteria for evaluating the appropriateness of the different steps of care, aiming at a consensus based on universally accepted indication for main variables

Table 1 Clinical data of the 142 records selected for the study

	Median or number of cases (%)	Range
Sex (M/F)	41/101	
Age (y)	36	16–76
Comorbidity		
Anxiety	56 (39.4)	
Depression	63 (44.4)	
Psychosis	25 (17.6)	
Neurological diseases	14 (9.9)	
Others	13 (9.2)	
Ingestion to admission time (minutes)	60	30–780
Undefined ingestion to admission time	21 (14.8)	
Undefined ingested drug	13 (9.2)	
Glasgow Coma Scale at entry (3-15)	14	4–15
Glasgow Coma Scale at disposal	15	9–15

considered.[1] To ensure independence, all experts were selected outside the area of Forlì. The local ethics committee of Morgagni Hospital approved the protocol.

Database

One author (AF) reviewed the clinical records of all consecutive adult subjects, who attended the ED of the community hospital of Forlì (50 000 visits per year) for suspected intentional drug overdose from December 1996 to March 2000, and submitted to a comprehensive drug screening (table 1).

Abstracted information included personal data, poisoning to admission time, type of suspected drug(s), comorbidity, signs and/or symptoms of clinical presentation, observation period, and clinical course. Cases with Glasgow Coma Score (GCS) <9 at time of disposal, and cases in whom lifesaving support was mandatory independently of laboratory results were excluded, as were patients with acute concomitant illnesses, suspected overdose by drugs of abuse or alcohol intoxication, unintentional drug poisoning, traumatic injuries, and chemical poisoning. Finally, records with insufficient data reporting and patients voluntarily discharged from ED were also excluded. According to these criteria, the clinical records of 142 patients were selected (table 1). These patients account for about 30% of all cases admitted for suspected drug poisoning in our institution, after exclusion of chemicals and carbon monoxide intoxication. In 82 cases (57.7%) the diagnosis was acute overdose on the basis of plasma or urine concentrations of drugs or their metabolites in amounts sufficient to explain the presenting symptoms. In 55 cases (38.7%) a single drug was responsible for acute intoxication, in the remaining 27 (19.0%) two or more drugs were found. The drugs more commonly involved were benzodiazepines (BDZ, 58 cases), neuroleptics (17 cases), other hypnotics (4 cases), tricyclic antidepressants (TCA, 13 cases), serotonine specific reuptake inhibitors (SSRI, 8 cases), non-tricyclic antidepressant (12 cases), anticonvulsants (12 cases), digoxin (2 cases), drugs of abuse (8 cases), analgesics (4 cases).

In 43 cases (30.3%), one or more drugs were detected, at trace levels. The most common drugs in this group were BDZ in 30 cases, neuroleptics (7 cases), TCA (5 cases), anticonvulsants (10 cases), antiparkinsonians (4 cases). In 17 patients (12.0%) no drug was detected at urinary Remedi screening (see below). Blood alcohol concentration >100 mg/dl was present in 34 cases (27 with drug overdose).

Gastrointestinal decontamination procedures were started in 59 cases soon after arrival at the emergency department, and this information was reported in the data sheet.

Study design

The drug screening had been performed in each case by means of an integrated system, combining a multi-column HPLC drug profiling system (Remedi HS Bio-Rad, Hercules, CA) and a fluorescence polarisation immunoassay (FPIA) with a TDx analyser (Abbott, Abbott Park, IL). In sequence, the protocol included the Remedi urine drug screening in all cases and, in case of drug detection, a confirmatory test with either Remedi in plasma or a quantitative FPIA, whenever available.[8–10] FPIA was carried out in plasma for drugs and in urine samples for drugs of misuse (opioids, cannabis, amphetamines, cocaine).

A combined analysis with Remedi in urine samples and plasma was performed in 37% of cases, whereas an additional quantitative confirmatory test with a single FPIA in plasma was necessary in 35% after the urinary Remedi screening.

The current library of Remedi HS multidrug profiling system permits the determination of over 900 common pharmaceutical agents and their metabolites, with a detection limit of 200 ng/ml.[9] This policy guarantees a final result in a turnaround time of 20–60 minutes. The system does not measure lithium, sulphonylureas, and most chemical agents.

The FPIA system permits the quantitative determination of plasma BDZ, digoxin, barbiturates, phenytoin, methotrexate, primidone, salicylates, paracetamol, theophylline, TCA, valproate, ethosuximide and the urinary detection of the commonest drugs of misuse (opioids, cannabis, cocaine, amphetamines). Blood alcohol concentration was measured by ALC, Dade Behring, Newark, NJ.

Data analysis

Median or mean values, standard deviations (SD), and frequencies were used to describe data distribution. For each outcome variable, the intraobserver agreement (reproducibility) between paired datasheets with/without the results of the drug screening was calculated using the chance corrected

Table 2 Reproducibility (intraobserver agreement; κ value) of disposal as function of drug screening

	Overall	A	B	C	D	E
Global agreement on disposal	0.233 (0.029)	0.403 (0.071)*	0.119 (0.064)	0.334 (0.076)	0.242 (0.060)	0.022 (0.048)*
Discharge	0.249 (0.036)	0.388 (0.076)	0.185 (0.077)	0.352 (0.086)	0.245 (0.085)	−0.012 (0.037)*
General ward	0.185 (0.037)	0.347 (0.075)	0.080 (0.080)	0.311 (0.082)	0.135 (0.081)	−0.032 (0.083)
HDU or ICU	0.290 (0.040)	0.641 (0.125)*	0.114 (0.093)	0.355 (0.014)	0.364 (0.070)	0.096 (0.062)*

*Significantly different from overall κ agreement (p<0.05). Data shown as mean (SE).

Table 3 Patients' disposal proposed by the five experts without and with the results of drug screening in the 142 patients admitted to ED for suspected drug overdose

	Screening not available (n=710)	Screening available (n=710)	p Value
Disposal			
Discharge	89 (12.5)	224 (31.5)	<0.001
General ward	437 (61.5)	400 (56.3)	0.136
HDU or ICU	184 (25.9)	86 (12.1)	<0.001

Percentages shown in parentheses.
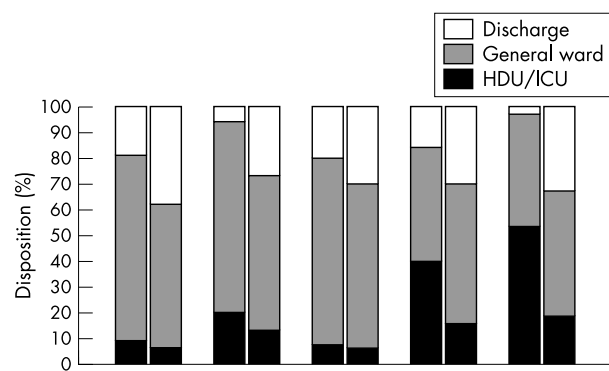
Figure 1 Opinion of the five individual experts (A, B, C, D, E) on appropriateness of disposal in relation to the availability of drug screening in patients admitted to the emergency department for suspected drug overdose. For each pair of columns, the left column refers to decision without the drug screening, the right column is with the drug screening available.

agreement index (κ).[11] After this, the interobserver agreement was also calculated using the same technique. A κ value of 0 indicates agreement no better than chance, and a value of 1 indicates perfect agreement. The degree of agreement was graded as follows: κ>0.75=excellent agreement, κ between 0.40 and 0.75=fair to good agreement, and κ<0.40=poor agreement.[12] Student's *t* test using standard error of κ estimates was used to determine the level of statistical significance of comparisons among κ values. Differences were considered significant when the two tailed p value was <0.05. Statistical analyses were performed running the SPSS/PC+ statistical package on a personal computer.[13]

RESULTS
Intraobserver reproducibility
The availability of drug screening significantly changed the physicians' opinion regarding patients' disposal. The overall reproducibility of the five experts when considering the same record with/without drug screening information was poor (0.233), as were the individual κ values for discharge after short observation (0.249), admission to general wards (0.185), and admission to HDU/ICU (0.290). Expert A and E had a significant non-homogeneous approach for disposal, expert A having a larger reproducibility on HDU/ICU admission, and

expert E having a lower reproducibility on HDU/ICU admission and discharge (table 2).

The analysis of the total 1420 records compiled by the five experts showed that the availability of drug screening would have saved a total of 135 of 621 hospital admissions (−21.7%; p<0.001), by increasing the number of patients discharged after a brief observation from 89 to 224 (p<0.001). In particular, the screening would have reduced the number of HDU/ICU admissions from 184 to 86 (−53.3%; p<0.001), and the total number of general ward admissions from 437 to 400 (−8.5%; p=0.136) (table 3). About 20% of patients were moved from HDU/ICU to general wards, and from general wards to discharge by all experts (fig 1).

Interobserver agreement
In the absence of drug screening, a very poor agreement was observed among physicians for disposal (κ=0.238). The results of drug screening significantly (p<0.001) improved the interobserver agreement to the fair to good range (κ=0.461) The agreement also increased when admission to an intensive care unit, to a general ward, and discharge from hospital were separately analysed (table 4).

DISCUSSION
The results of this study suggest that comprehensive drug screening affects clinical decision making for patients attending the ED for suspected intentional drug overdose in terms of use of hospital resources.

The usefulness of a multidrug analysis in the management of patients with acute drug poisoning has not been resolved. Several authors claim that comprehensive drug screenings are useful for the treatment of their patients, influencing their management, but most studies do not provide quantitative evidence to support this conclusion.[2 8 10 14–16] Earlier studies have suggested that unexpected laboratory findings scarcely influence management or outcome of patients with drug overdose.[5 6 17] Similarly, laboratory evidence of a clinically unsuspected drug does not seem to serve as a useful marker for severity of illness and does not, in itself, identify patients requiring closer observation or having poorer prognosis.[18] One possible reason for benefits of laboratory results may be that they reassure the physician. The implicit psychological benefits, which are not easily quantified, seem to be inversely correlated with physician's experience and confidence.[19] On the other hand, other studies concluded that laboratory results

Table 4 Interobserver agreement (κ value) on ED disposal as function of drug screening availability in the 142 patients with suspected drug overdose

	Overall	Screening not available	Screening available	p Value
Global agreement on disposal	0.358 (0.014)	0.238 (0.019)	0.461 (0.020)	<0.001
Discharge	0.459 (0.017)	0.319 (0.031)	0.488 (0.021)	<0.001
General ward	0.343 (0.012)	0.261 (0.016)	0.428 (0.019)	<0.001
HDU or ICU	0.398 (0.018)	0.296 (0.020)	0.578 (0.032)	<0.001

Data shown as mean (SE).

have only a limited role in the management of the acutely poisoned patient, the clinical course remaining the leading criterion.[3] [4]

How can a screening test demonstrate its usefulness? We have a reliable comprehensive drug identification system, testing over 900 drugs in blood and urine in our unit.[9] In the absence of any unequivocal gold standard, we only simulated in a table top comparison the clinical position of an emergency physician when dealing with a patient with suspected drug overdose, and evaluated if the screening influenced decision making, independently of clinical data.

The decision on patients' disposal may be critical in borderline cases. The clinical course of patients with suspected drug overdose can be predicted during the first few hours of observation, sufficient to identify low risk patients.[19] However, without laboratory results, physicians are prone to overestimate the likelihood of late deterioration after drug overdose, and may be reluctant to take risks whenever a minimum of uncertainty exists, leading to over-treatment and inappropriate disposal. This is perceived as a less serious error than not admitting a patient who could benefit by continuing hospital care. However, the shortage of hospital resources implies that any attempt to reduce inappropriate clinical care must be pursued.

Our simulated study demonstrates that this drug screening may be relevant for the medical management of patients with suspected drug overdose, improving the physicians' agreement on the use of resources. Our experts were well trained in emergency medicine, but not specifically trained in medical toxicology. Therefore, our data may be extrapolated to the majority of emergency departments, where physicians have only a basic knowledge of clinical toxicology.

Our protocol has obvious limitations. All relevant information was included in paired data sheets submitted to external experts, but visiting a patient is different from revising a clinical record. Physicians do not always behave the way they say they would have behaved, but in paired analysis this is not expected to bias the final results, unless relevant data were omitted. It is also conceivable that the non-homogeneous experience of experts with our comprehensive drug screening may have led them to overestimate its significance. Finally, a discussion between physicians and analysts is frequently needed to correctly interpret the results of drug screening. In the hands of non-expert physicians, comprehensive screening even detecting minimum amounts of drugs might lead to an overestimate of the results, as the detection of the presence of drugs does not necessarily imply causation. Apparently, in the present series the potential bias for "false positive" results ended up in reducing the use of resources. This implies that the busy physician is more ready to accept the "true negative" data than the "false positive" results.

We now need to know whether this result may be reproduced in the clinical setting, improving the final outcome of patients admitted to ED for suspected intentional drug overdose, and whether this policy is cost effective. The cost of each test varies between €120 and €150 depending on the need for and number of confirmatory tests. This compares favourably with the potential reduction hospital admission, but the appropriateness of this policy on final outcome needs to be demonstrated. Our results are the basis for prospective, controlled studies on indications, limits, usefulness, and cost effectiveness of the comprehensive drug screening.

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